WASHINGTON NEWS

Report of Council on Aging . .
A. M. A. Backs Tax Relief for Aged . .
Kefauver Drug Hearings . .

REPORT OF COUNCIL ON AGING

The cabinet-level Federal Council on Aging told President Eisenhower that the problems of the elderly cannot be solved through standard "overnight" remedies.

In the council's first report to the President the group declared that "It will be by a steady and objective scrutiny of needs, and a realistic matching of them with resources, that a continuing contribution to improving the well-being of older people will be assured."

The council, headed by Arthur S. Flemming, secretary of Health, Education and Welfare, said there is "growing concern" about the problem older persons with low incomes have in paying for modern medical care. It endorsed further study by the Social Security Administration of ways of encouraging the development of coverage under voluntary plans and "such ways to supplement these plans as may be found practicable and desirable."

The coverage of voluntary plans "has been consistently increasing," the council pointed out.

"There is an urgent need," according to the report, "to stimulate and support community health services for the aged and chronically ill, in which public and private agencies and professional persons are all joined in action.

"The types of programs needed include out-of-hospital care such as home care services, homemaker services, [and] nursing homes; early restorative medical services; and promotion of the health of the aged by such methods as screening clinics, nutrition programs, and health appraisals."

One of the major problems is that of employment barriers to older persons, the council reported. Calling for vigorous educational efforts to combat discriminatory practices, the group said there should be no formal recommendations for action in this field until after the 1961 White House Conference on Aging.

Elderly persons with fixed incomes are hit especially hard by inflation, the report said, adding that "fiscal and monetary policies that prevent erosion of the dollar are essential to the economic well-being of all of us, but especially to older people on fixed income."

Noting the various problems often linked with old age, the council said, "These conditions are not to be thrown together to suggest a single great dilemma in which all persons are likely to find themselves upon reaching a certain age." Because each of these problems, such as inadequate income, "reaches on into all age levels, to one degree or another, they cannot realistically be grouped together, distinguished by an arbitrary age break, *and labeled as the common problems of older people.*"

Part of the council's report was a summary of federal activities in the field of aging. It noted that more than 70% of persons aged 65 and over are now receiving payments through the social security retirement and disability programs and the old-age assistance programs. Over-all income maintenance payments to the elderly by the federal government have risen from 2.5 billion dollars in 1950 to 14 billion dollars estimated for next year.

In addition to HEW Secretary Flemming, the council is composed of the secretaries of Treasury, Agriculture, Commerce, and Labor; and the Administrators of Housing and Veterans Affairs.

In releasing the report, Flemming told reporters that the administration so far had not formed any alternate plan to the proposal in Congress to extend the social security program to partly finance health care for the aged. He said efforts were still going on to arrive at some sort of an aid program for private insurance carriers but predicted that no program along these lines will be ready for the next Congress.

In making his statements Flemming renewed the administration's opposition to the so-called Forand social security bill, which he said would doom private health insurance coverage of the elderly.

The HEW Secretary indicated that the administration will offer some type of program to cover this point at the next Congress but stated that no decision has been made yet on what type of program it would be.

A. M. A. BACKS TAX RELIEF FOR ELDERLY PERSONS

The American Medical Association, in a statement presented to the House Ways and Means Committee, declared that a partial solution of the economic problems of the elderly would be further tax deductions. Dr. F. J. L. Blasingame, Executive Vice-president of the A. M. A., said, "Such a pro-

(Continued on next page)

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Riseman, J. E. F., *et al.*: Circulation *17*:22, 1958

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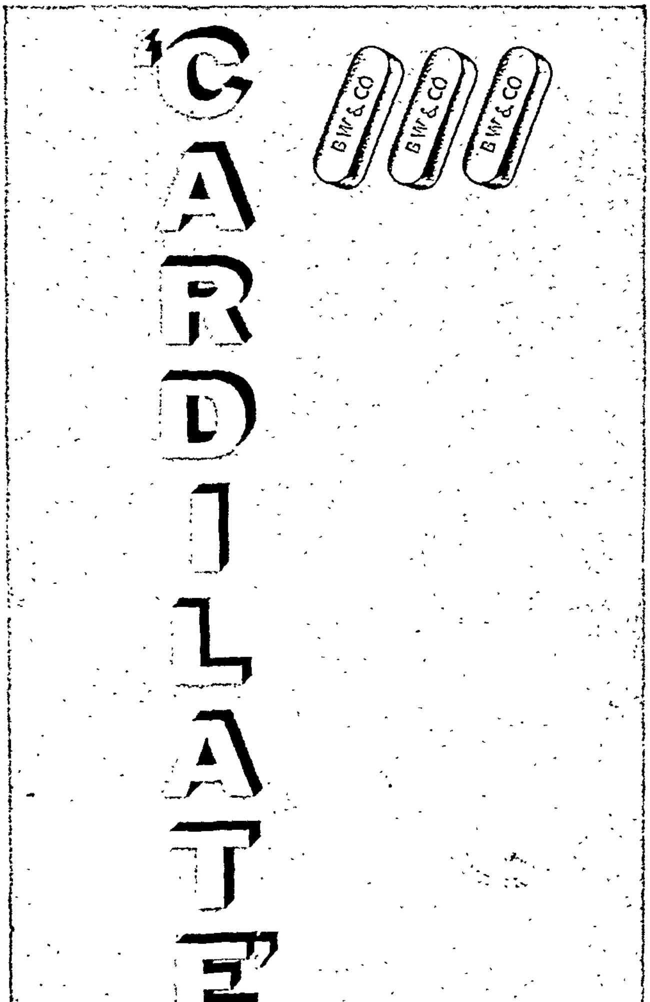


gram would facilitate the provision of health care on an individually financed basis, without the dangers implicit in the adoption of a federal system of hospitalization and medical care."

Noting that there were legislative proposals before the Committee to provide federally financed medical and hospital care for social security beneficiaries, Dr. Blasingame declared, "To the extent that the health care problems of the aged are economic in nature, we believe that a partial solution may be provided through a more liberal tax deduction program for persons over . . . 65."

The A. M. A. official also renewed the organization's backing of the House-passed measure offering tax incentives for self-employed persons who invest money in retirement plans to place them on an equal footing in this regard with salaried employes. "The physicians, dentists, farmers, lawyers, architects, veterinarians, merchants and many others who comprise the nation's self-employed have long been neglected in federal tax legislation relating to pensions," said Dr. Blasingame.

"With high taxes and inflated living costs, it is difficult for persons in these occupations to set aside adequate funds for retirement without a tax deferment similar to that available to corporate employees," he said.

The House last year approved the bill, sponsored by Rep. Eugene J. Keogh (D., N. Y.) and Rep. Richard M. Simpson (R., Pa.), but the Senate did not act on it.

Dr. Blasingame also told the Committee that "graduated income tax rates which reach confiscatory levels are especially unfair to professional people and others who derive their income from services which they personally perform." He pointed out that special treatment for the taxation of capital gains and other types of credits, deductions, and allowances "have tended to soften the effect of graduated taxes with reference to income earned from sources other than the rendition of personal services."

"We believe that a simplification of our system of taxation so as to permit lower rates for all is seriously needed," he said.

The Ways and Means Committee, headed by Rep. Wilbur Mills (D., Ark.), is studying the overall tax structure to determine whether the tax base might be broadened and taxes generally lowered by closing possible loopholes and eliminating any unfair advantages.

DRUG HEARINGS OPEN

Sen. Estes Kefauver (D., Tenn.), chairman of a Senate judiciary subcommittee studying the drug industry, said the week of hearings starting on Dec. 7 would deal with drugs used in the treatment of arthritis and related illnesses that often afflict elderly persons. He said the subcommittee later will go into more general aspects of the manufacture of drugs. He said the subcommittee's investigation probably would continue through next spring.

"We have the very finest medicines in the world," the senator told a news conference, "but we are very much concerned that the prices are so high they may be unavailable to many people."

The subcommittee does not plan to investigate retail prices, he said, only manufacturers' prices. Areas of inquiry include the question of monopoly, the patent process for drugs, the financial relationships between drug manufacturers and financial institutions, and the effect on small companies of promotional campaigns by large companies.

Kefauver said officials of 20 major drug companies, in addition to the other witnesses, would testify during the course of the investigation.

Among the first week's scheduled witnesses were spokesmen for Schering Corporation, Merck & Co., Inc., and the Upjohn Company, which Kefauver said were the principal manufacturers of steroid hormones, or cortisone derivatives, used in the treatment of arthritis.

MISCELLANY

The National Institutes of Health reported that 1,040 research grants and 165 fellowships totaling $18,600,000 were awarded during October of this year. Of the month's total, $9,700,000 was allocated to support 679 new research grants and fellowship awards. The rest was for the continuation of previously approved grants and awards.

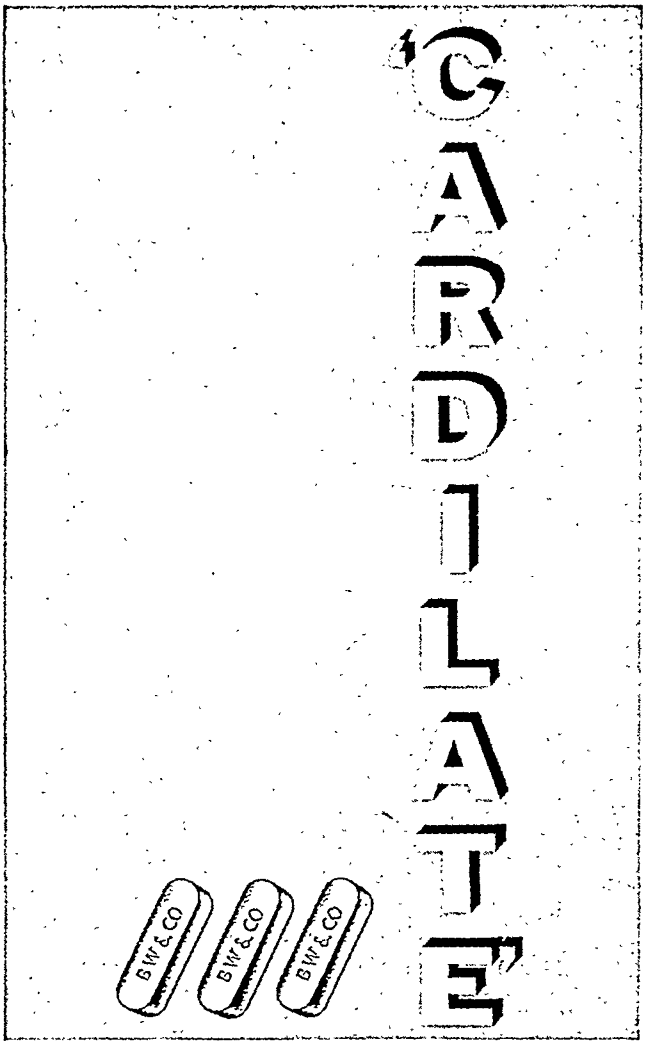
The U. S. Public Health Service reported the award of 82 grants totaling $16,100,000 to help build and equip health research facilities in 72 institutions across the nation. The program, authorized at 30 million dollars annually, is designed to extend and improve medical research facilities.

The Civil Service Commission allowed federal agencies to increase pay rates for physicians starting government service. Entrants may now receive top pay scale for their grade category rather than start at a minimum scale and work to the top of a grade. The CSC may raise starting rates in the case of hard-to-fill positions.

The Internal Revenue Service notified Blue Cross-Blue Shield plans that a separate tax form (1099) must be furnished by the plans for all physicians to whom they make payments of $600 or more in any taxable year.

A Public Health Service official, Dr. William J. Brown of the Communicable Disease Center, Atlanta, Ga., said there is evidence suggesting a steady rise in the incidence of venereal disease since 1954. He blamed in part false confidence by the general public that penicillin alone could eradicate gonorrhea and syphilis.

The National Retired Teachers Association and the American Association of Retired Persons said they are making a cut-rate drug service available to all Americans over 65 years of age if they place their orders with the service's mail order centers in Washington, D. C., and Altadena, Calif.



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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

November

American Academy for Cerebral Palsy, Statler Hilton Hotel, Los Angeles, Nov. 30-Dec. 2. Dr. Glidden L. Brooks, Brown University, Providence 12, R. I., Secretary.

American College of Chest Physicians, Dallas, Texas, Nov. 29-30. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Secretary.

National Society for Crippled Children and Adults, Palmer House, Chicago, Nov. 29-Dec. 2. Dr. Dean W. Roberts, 2023 W. Ogden Ave., Chicago 12, Executive Director.

Puerto Rico Medical Association, Santurce, Nov. 24-28. Mr. J. A. Sanchez, Box 9111, Santurce 29, Puerto Rico, Executive Secretary.

December

American Academy of Dermatology and Syphilology, Palmer House, Chicago, Dec. 5-10. Dr. Robert R. Kierland, First National Bank Bldg., Rochester, Minn., Secretary-Treasurer.

American Association for the Advancement of Science, Morrison Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. of Virginia, Richmond, Va., Director of Public Information.

American Psychoanalytic Association, Biltmore Hotel, New York City, Dec. 4-6. Dr. David Beres, 151 Central Park West, New York 23, Secretary.

American Rheumatism Association, Henry Ford Hospital, Detroit, Michigan, Dec. 11. Gerard W. Speyer, 10 Columbus Circle, New York 19, Executive Secretary.

Association for Research in Nervous and Mental Disease, Inc., Hotel Roosevelt, New York City, Dec. 11-12. Dr. Rollo J. Masselink, 700 W. 168th St., New York 32, Secretary-Treasurer.

First Annual Graduate Medical Education Conference-Residency Training Program, Univ. of Pennsylvania, Philadelphia, Dec. 3-4. Dr. Alfred S. Frobese, Graduate School of Medicine, U. of Pennsylvania, Philadelphia 3, Chairman.

Medical Society of the United States & Mexico, Valley Ho Hotel, Scottsdale, Ariz., Dec. 2-4 (followed by two-day session Desert Inn, Las Vegas, Nev.). Dr. A. H. Tallakson, 2025 N. Central Ave., Phoenix, Ariz., Convention Co-Chairman.

New York Heart Association, Symposium on Salt and Water Metabolism, Biltmore Hotel, New York City, Dec. 11-12. Dr. Alfred P. Fishman, N. Y. Heart Association, 10 Columbus Circle, New York City, Chairman.

New York State Society of Anesthesiologists, Inc., Postgraduate Assembly in Anesthesiology, Hotel New Yorker, New York City, Dec. 9-12. Dr. Edwin J. DePolo, 131 W. 11th St., New York 11, Secretary.

Southern Surgical Association, The Homestead, Hot Springs, Va., Dec. 8-10. Dr. John D. Martin Jr., Emory Univ., Box 459, Atlanta 22, Ga., Secretary.

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Mid-Winter Clinical Convention for Ophthalmologists and Otolaryngologists (29th), Research Study Club, Ambassador Hotel, Los Angeles, Jan. 17-22. Dr. Norman Jesberg, 500 S. Lucas Ave., Los Angeles 17, Secretary-Treasurer.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel, Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago, Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-Treasurer.

American Academy of General Practice, Philadelphia, Mar. 19-24. Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, Mo., Executive Director.

American Association for the History of Medicine, Inc., Charleston, S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Institution, Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broadmoor, Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Portland Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, New Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ. of Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. 30. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Treasurer.

American Laryngological Association, Deauville Hotel, Miami Beach, Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of Technology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Society, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Fla., Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minneapolis 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, Montreal, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, N. Y., Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Rico, Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory University, Atlanta 22, Ga., Secretary.

Missouri State Medical Association, Sheraton-Jefferson Hotel, St. Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Louis 3, Executive Secretary.

National Health Council, National Health Forum, Miami, Fla., Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, Executive Director.

National Multiple Sclerosis Society, New York City, Mar. 8. Mr. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Mar. 30-Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimore 1, Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel, New Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave., New Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, Mar. 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Executive Secretary.

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CAUSATION, PREVENTION, AND CONTROL OF ACCIDENTAL POISONING

Harold Jacobziner, M.D., New York

The New York Poison Control Center, established in 1955, accumulated reports on 23,862 incidents of poisoning until the end of 1958. Among the 13,069 patients under the age of 20 there were 70 deaths, and 51 of the deaths in this group were caused by lead poisoning. In this age group aspirin accounted for 15.7% of the cases, but the data also attested to the frequency with which tranquilizers are now found in the home. Nearly all the reported incidents were preventable, and nearly one-third of them could have been prevented by proper storage and handling of five leading products. The poison control center has become an important source of information for the treatment of poisonings, but for success in prevention a program of education for the public is necessary. The physician, as a key member of the poison control team, can make a significant contribution in solving this problem.

THERE has been an increasing awareness in recent years of the importance of accidental chemical poisonings as a cause of death and disability. More children under 5 years of age died last year in New York City from accidental chemical poisonings than from diphtheria, poliomyelitis, rheumatic fever, scarlet fever, and other streptococcic infections combined. Fourteen hundred fifty deaths were reported in the United States last year from poisonings by agents other than poison gases and spoiled food. Over 400 of these deaths were in children under 5 years of age.[1] The alarming increase in both fatal and nonfatal poisonings is related to the rise in new products and to the increase in the population at risk.

Control

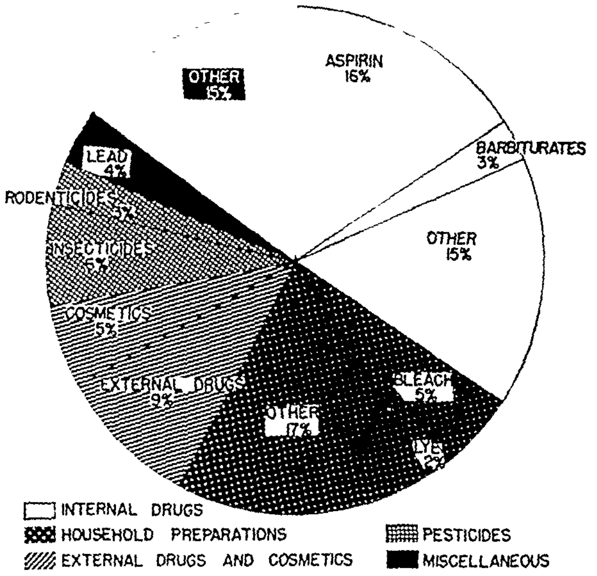
As a result of stimulus from the American Academy of Pediatrics, the New York Academy of Medicine, and local medical societies a Poison Control Center was established in March, 1955, in New York City as a regular activity of the department of health.[2] The center is a regional facility and does not limit its services to New York City. It serves many communities in upstate New York, New Jersey, and Pennsylvania, and calls are often received from every section of the United States and at times from foreign countries. Last month 86 calls for assistance were received from 40 cities in New York state, from 17 in New Jersey, and the rest from cities in Connecticut and Pennsylvania.

Personnel.—All of the 146 hospitals with emergency services have appointed a staff physician to serve as a poison control officer. He is responsible for liaison with the Poison Control Center and for the poison control program within his own hospital.

Assistant Commissioner, New York City Department of Health.

Read before the Section on Pediatrics at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1959.

The network of poison control officers within hospitals has proved to be a useful device as a "ready mobilization force" in alerting hospitals and the profession about an imminent "nonpoisoning" danger or when quick action is required. It has been used in alerting hospitals about outbreaks of food poisoning and other imminent danger signs. The network has also been used successfully with the poliomyelitis immunization programs within hospitals. A more recent use and involvement of this network was with regard to the over-all accident prevention program; initiated by the academy of pediatrics in our region. The complete roster was made available to the local chairman and the entire network of hospital poison control officers was utilized to spearhead safety programs within their respective localities.



Analysis of 13,069 reported cases of poisoning in persons under 20 years of age, in New York City, 1955-1958, by type of poison.

Reporting of Poisonings.—A "poisoning" as used here is defined broadly as "an abnormal ingestion, absorption, or inhalation of a substance which may produce untoward symptoms or toxic manifestations." Poisonings are reported by physicians and hospitals on a prescribed form immediately after occurrence. After discharge or on completion of treatment of the patient, hospitals and physicians report promptly on a designated form additional data about the symptoms, treatment, and outcome of the poisoning. In order to obtain more complete information about the mode of occurrence, environmental background, activity at time of accident, and possible contributing factors leading to the occurrence, and to impart guidance to the family in the prevention of future accidents, a home interview is made by a public health nurse or public health sanitarian. Data from this investigation are recorded on a five-page form specifically designed for this purpose. A complete register and tabulations are kept on each hospital and for each product as well as for each patient. The center also maintains a comprehensive library on recent advances in pharmacology, toxicology, and new products and their uses.

Epidemiology of Poisonings.—Gordon [3] aptly emphasized that accidents follow the same pattern as disease processes. If any significant gains are to be made in the control and prevention of accidental poisonings, more knowledge about the natural history of accidental poisonings is needed. A careful analysis of facts obtained is essential before a sound control program can be formulated and implemented. All three components—the agent, host, and environment; the mode of occurrence; and the interrelationships and the interactions of these—must be studied. We must know how poisonings happen, where, when, to whom, and why. Populations at risk, injurious agents, and unsafe environments must be identified and defined.

To obtain such information, the New York City Poison Control Center is gathering data on a continuing basis on all reported incidents through use of the essential tools of epidemiology, which have proved eminently successful in the control of communicable and infectious diseases. Data are analyzed by type of poison; age, sex, and color of patient; locale; season; mode of occurrence; type of activity at time of accident; supervision; contributing and related factors; severity; whether self-administered; type of treatment; symptoms; amount ingested; onset; outcome; preventability; accident proneness of patient; relation to availability and accessibility; and many other factors. The household interview questionnaire contains over 40 questions relating to the natural history of the poisoning. It serves as a basis for considerable factual information about the etiology and pathogenesis of accidental chemical poisonings, including the physical, cultural, and social family environment. From March 9, 1955, to the end of December, 1958, 23,862 incidents of poisonings were reported.

Agents Responsible for Accidental Chemical Poisonings.—Over 300 individual products, many containing a variety of ingredients, were the causative agents. For the sake of simplicity they are classified in five major groupings, as shown in the figure.

Internally taken drugs caused nearly 50% of all poisonings, barbiturates and aspirin being the main offenders. Household preparations were the second leading cause. These products are generally not considered "poisonous" in the average American household and are easily accessible to young children, causing a large number of fatal and nonfatal poisonings.

Type of Poisoning

Of all poisonings 54.7% occurred in persons under 20 years of age. The first three major categories of poisonous substances, i. e., internally taken drugs, household preparations, and externally applied drugs and cosmetics, were responsible for 72.1% of all reported poisonings in persons under 20 years of age.

While no age group is exempt from accidental poisonings, young children constitute a highly susceptible and vulnerable group. Children under 5 years of age constitute about 8% of the total population of New York City, but they contributed 46.2% of all poisonings reported at all ages.

Of the 13,069 poisonings reported in persons under 20 years of age the under-5 age group accounted for 84.4% of all cases. In persons aged under 20, 2 years was the age of highest risk, children aged 2 contributing 4,042 incidents or 30.8% of the total poisonings in this group. One-year-old children followed closely behind with 3,634, or 27.9% of poisonings. Children at the ages of 1, 2, and 3 years contributed a combined total of 9,585 episodes, 73.3% of all reported poisonings in the under-20 age group (see table). The high frequency of poisonings in the first four years of life is undoubtedly related to a lack of adequate supervision, lack of caution and experience, careless handling and storing of materials, and ready availability and accessibility. With advancing age, as the child gains from education and experience and becomes more cautious, there is a precipitous decline in the incidence of poisonings.

Poisonings in Persons Under Twenty Years of Age in New York City, 1955-1958

	Age, Yr.									
Type of Poison	Under 1	1	2	3	4	5-9	10-14	15-19	Total	%
Internally taken medicaments	108	602	1,565	911	333	206	171	522	4,448	34.0
Aspirin	28	183	864	553	167	59	49	158	2,061	15.7
Barbiturates	10	45	100	16	22	23	34	98	378	2.9
Other	70	371	601	342	141	124	88	266	2,009	15.4
Externally applied medicaments	91	332	302	139	57	103	45	120	1,192	9.1
Cosmetics	58	214	259	89	31	19	7	22	699	5.3
Household preparations	127	928	670	235	115	109	42	121	2,347	18.0
Bleaches	28	222	179	69	39	31	19	72	659	5.0
Lye	8	60	55	48	29	22	7	11	240	1.8
Other	91	616	436	118	47	56	16	38	1,448	11.1
Solvents	38	317	208	60	26	32	14	41	736	5.6
Turpentine	8	69	46	11	4	9	2	6	155	1.2
Kerosene	9	78	44	9	5	3	1	3	152	1.2
Other	21	170	118	40	17	20	11	32	429	3.3
Insecticides	73	321	226	82	49	45	4	39	839	6.4
Rodenticides	28	133	90	48	22	15	3	21	360	2.8
Miscellaneous	153	787	722	315	139	199	77	56	2,448	18.8
Lead	4	120	184	89	28	25	3	0	453	3.5
Other	149	667	538	226	111	174	74	56	1,995	15.3
Total	679	3,634	4,042	1,909	772	728	363	942	13,069	
%	5.2	27.9	30.8	14.6	5.9	5.6	2.8	7.2	100.0	

Growth, Development, and Type of Poison.—The type of poison varies with a child's stage of growth and development. Children of one year of age and under are likely to ingest poisons found at low levels, on the floor, under the sink, and on low shelves. At this age they still crawl about and are unable to climb to high levels. They are undiscriminating explorers and "mouthers." The poisonous substances they are thus most likely to ingest are household preparations such as cleaning, sanitizing, and polishing agents: solvents; and pesticides. At 2, 3, and 4 years of age, as the child becomes more mobile and able to climb to higher places, he is more likely to ingest poisons stored at higher places such as "internally taken medicaments" which may be found in medicine cabinets and drawers and on top of bureaus, open shelves, television sets, and other such storage places. The medicaments are usually the ones prescribed for adult members of the household but which are carelessly stored in unsafe places and within easy access of the victims.[1]

No significant difference in incidence between the sexes was found, and no difference was found among various ethnic groups which could not be attributed to socioeconomic rather than constitutional factors.

Leading Toxic Agents.—Although the number of products incriminated in the 13,069 poisonings is legion, five leading products were responsible for 30% of the total poisonings in this group. Thus, had ordinary precautionary measures been used in the storage and handling of these five substances alone, nearly one-third of all poisonings in persons aged under 20 might have been prevented.

Aspirin accounted for 2,061 cases, 16% of the total. The flavored aspirin preparations for babies were most frequently incriminated, chiefly because of their common use in the home. The most frequent victims of aspirin poisonings were children

2 and 3 years of age. Children these ages contributed 1,417 cases or approximately 69% of all aspirin poisonings in the under-20 age group.

Bleaches were the cause of poisoning in 659 cases in persons under 20 years of age. Children at 1 and 2 years of age were the most frequent victims of poisoning by bleaches. Children of those two ages, together, accounted for over 60% of the total in this group. Household liquid bleaches in general have not proved a serious problem in therapy and outcome because most patients who ingest them respond to gastric lavage and induced vomiting. The usual content of sodium hypochlorite is about 5% and the pH is generally not too high. However, one must be cautioned against thinking that all chlorine bleaches are mild; the high-chlorine compounds such as "HTH," with 65% available chlorine, could cause serious corrosion, permanent injury, and death.

Lead is a frequent cause of poisoning in children. It accounted for 453 cases and 51 deaths in this series, a case fatality rate of 11.2%. Last year 114 cases were reported in New York City and 21 of these had a fatal outcome. Over 92% of the patients were under 4 years of age. A sex difference was also noted, the ratio of female to male being 63:51. This higher incidence in females was noted in all ethnic groups.[5] Only 24 (21%) of the children were white, which is in marked contrast to the general population, which is about 75% white. The racial disparity is undoubtedly a reflection of socioeconomic conditions, although a factor responsible for the high incidence in nonwhite and Puerto Rican neighborhoods is perhaps the fact that hospitals in these areas have become keenly aware of this problem and are diagnosing such poisonings with greater frequency.

Of the cases 65% occurred during the months of July, August, September, and October. It has been postulated that metabolic disturbances, increased lead absorption, and dehydration may be influencing factors. However, the exact cause for the seasonal variation is still unknown.

Pica and Lead Poisoning: The close association of lead poisoning with pica has been observed.[5] Blood lead level determinations in all children with pica and their siblings is recommended. It is a technique which can be employed with profit in both private and clinic practice. Some children, particularly siblings of children with lead poisoning and pica, although entirely asymptomatic may show evidence of lead intoxication in laboratory blood and urine lead level investigations. The blood should also be examined for anemia and basophilic stippling. An x-ray examination of the long bones and abdomen and a qualitative test for coproporphyrin in the urine is also helpful. All children with pica, with normal blood lead levels, i. e., of less than 0.06 mg. per 100 cc. of blood, who are asymptomatic, should be periodically observed and carefully examined for possible evidence of lead intoxication.

Prevention to exposure and reexposure is the best therapy. Parents are to be alerted to the harmful effects of children's chewing paint containing lead and told to avoid its use for indoor painting, to remove the old paint completely, and to replaster and repaint the apartment with lead-free paint. Although all reported cases of lead poisoning in children in New York City resulted from the ingestion of painted wall plaster or paint from window sills and paint droppings from ceilings and walls, attention has recently been called to glazed dishes as a possible source of lead poisoning.[6] It is puzzling why lead poisoning, which causes more deaths than any other type of accidental poisoning, does not receive the attention it deserves.

Barbiturates: While over 17% of all poisonings at all ages were due to barbiturates, these products were responsible for only 3% of all poisonings in persons aged under 20. A total of 378 incidents was reported in this age group. The highest incidence occurred in those aged 2 and 3 (nearly 39% of the total). The medicament was usually prescribed for an adult member of the family, often for grandparents, and obtained by children from pocketbooks, medicine cabinets, or low shelves. Five fatalities resulted from ingestion of barbiturates by children in this group. One death occurred in a child aged under 4.

There is still considerable difference of opinion about the preferred treatment in barbiturate poisonings.[7] While some recommend therapy with analeptics, others insist that the best results are obtained with supportive therapy and careful attention to respiration and maintenance of circulation, electrolyte balance, and good nursing care. Some warn that analeptics may increase the danger of narcosis by causing convulsions, cardiac irregularities, and vomiting. I have had reports of favorable outcome with both modes of therapy.

Lye: Lye was responsible for 240 incidents, 2% of all poisonings in persons aged under 20, the highest incidence being in those aged 1 to 3 years, 68% of the total reported. While there were no fatalities in this series, esophageal burns and strictures were common. Some authorities believe that, whenever a child ingests any amount of a potentially dangerous caustic or corrosive agent, the esophageal mucosa is damaged. For this reason they recommend that treatment of such children be carried out expectantly rather than delayed until a stricture develops.[8]

Methyl salicylate and carbon tetrachloride together caused 229 incidents and 23 fatalities. These products, which are very hazardous, could easily be replaced in the home by much safer and equally effective substitutes. Their use in the home should be vigorously discouraged.

Influencing Factors

The relation of availability to accidental poisoning is well illustrated by the increasing number of poisonings due to tranquilizing agents. While in 1955 only 9 such incidents were reported, in 1958 the number increased to 273. Again the highest incidence was in children aged 2. This reflects the increased frequency with which these are now found in the home.

Location.—In previous studies[9] it was found that more than 80% of the substances involved in poisonings were placed by adults where they could be easily reached by children, such as at low levels, on the floor, under the sink, in dresser drawers, in open closets, on open shelves, on bedroom furniture, on television sets, and in handbags. In a random sample of 1,000 poisonings in persons aged under 20 reported during 1958, 83% of the substances were so placed and in 17% the exact location was unknown. The kitchen was the most dangerous place, accounting for 30.2% of all poisonings in this series. The bedroom was the place of poisoning in an additional 24.4% and the bathroom in 10%.

Original Container.—Of the families interviewed 20% did not consider the toxic agent involved in the poisoning as hazardous. In 36.7% of the poisonings the agent was not in its original container. This varied greatly with the toxic agent involved. Internally taken and externally applied medicaments were generally in their original containers, but the reverse was true of the household products, bleaches, insecticides, rodenticides, and petroleum distillates. These products were frequently placed in household utensils such as cola bottles, drinking glasses, mayonnaise jars, saucers, and milk bottles. Many substances such as benzene, turpentine, and carbon tetrachloride were left after use in household utensils and often mistaken by children for food or water and thus accidentally ingested. It is also the practice among certain groups to buy large quantities of a product and redistribute it in unlabeled household containers to other families in the tenement house or to friends. Such careless handling and storing is responsible for many needless chemical poisonings.

Characteristics of Families of Children Involved in Poisonings.—The more economically deprived areas had the highest incidence. Nearly 32% of the fathers were laborers. The educational level of the family was classified as "medium" by the visiting public health nurse in 57.6% of the cases. This was in close correlation with the socioeconomic level, which was reported as "medium" in 56.3% and "low" in 25.6% of the cases.

At the time of the accident, the child was under direct supervision of an adult family member in 72.6% of cases. The accident happened, however, with lightning rapidity when the adult member was distracted for a moment to answer the doorbell or a telephone call or the child strayed into a different room.

Time of Day.—Of all poisonings in this group 75.3% occurred between the hours of 6 a. m. and 5 p. m. Except for lead, possibly aspirin, naphthalene, and Christmas-tree ornaments there was no seasonal pattern to be observed in the type of poisonous substance ingested.

Growth, Development, and Behavior Pattern.—Of the children in this group 66.8% were judged by their parents to be average in comparison with other siblings; 73% were said to be of average intelligence and 11.6% were judged as having above average intelligence. Seventy-two per cent were classified as active and curious and 14.0% as mischievous. Many were listed as having a combination of all three patterns. Admittedly, these observations are subjective in character and thus subject to error.

Accident Proneness: In only 10% was a history of a previous accident to the patient elicited. In 14% a history of a previous accident to another member of the family was obtained.

Recognition, Treatment, and Prevention

Signs, Symptoms, and Treatment of Poisonings.—The symptoms most frequently encountered were burning in mouth and throat, vomiting, nausea, abdominal pains, and stupor. In 42% no signs or symptoms were reported. Only 5.2% of the poisonings were classified as severe, 57.5% were said to be mild, and 21.7% were of moderate severity.

Seventy-two and seven-tenths per cent were treated by lavage or induced vomiting, or both, either alone or with supportive therapy. About 70% were treated in hospital facilities. Included in this group were 25% of children who were admitted to the hospital inpatient service. Nearly 49% remained in the hospital up to three days and another 16% between four and seven days.

Fatalities.—Seventy deaths occurred in 13,069 patients who were known to be under 20 years of age, about one fatality for every 200 nonfatal cases. The fatality rate is heavily weighted with lead poisoning, which contributed 51 deaths or nearly 73% of all fatalities in this group. If all lead poisonings were excluded, both incidents and fatalities, the ratio of fatal to nonfatal poisonings would be 1:664. This approximates the findings of the National Clearinghouse for Poison Control Centers.

Preventability.—Except for attempted suicides, the public health nurse who visited the homes commented that the accident was preventable. A careful review by me of the mode of occurrence in each case also disclosed that nearly all reported incidents were preventable, if ordinary precautionary measures had been employed in the storage and handling of the incriminated products.

Antidote Myth.—There is, unfortunately, a widespread belief that an antidote is available for every type of poisoning. As a matter of fact, there are only a handful of specific and effective antidotes. Forney [10] mentioned dimercaprol as an antidote for arsenic, nalorphine as an antidote for morphine and morphine-like compounds, ethylenediaminetetraacetic acid (EDTAA) as an antidote for heavy metals like lead, and penicillamine for promoting rapid urinary elimination of copper, iron, or lead. Vitamin K is effectively used as an antidote for anticoagulant rodenticides. Lacking specific antidotes the most effective plan is rapid elimination of the toxic substance before it is absorbed. In most instances this can be accomplished by dilution and evacuation, by means of induced vomiting and prompt gastric lavage, except where this is contraindicated such as in cases of poisoning with corrosives and kerosene and other petroleum products and when the patient is in deep coma or having convulsions.

In a recent survey of hemodialysis facilities available in the United States and Canada made by us for the American Academy of Pediatrics, it became apparent that this lifesaving measure is perhaps not used as widely as it should be for severe dialyzable and nephrotoxic poisonings in children. Of 2,970 cases treated with hemodialysis, only 82 were in children.

Exchange transfusions have also been used effectively in methyl salicylate, boric acid, and aspirin poisonings.[11] This method is valuable in the treatment of ingestion of poisons which cause marked destruction of red blood cells. In a recent presentation before the American Pediatric Society,[12] based on an evaluative study, alkalinization of the urine through an infusion of sodium bicarbonate was recommended as an effective therapeutic agent in the management of salicylate poisoning. The rate of elimination of salicylate from the body and the decrease in plasma salicylate level achieved by this mode of therapy are claimed to be as good as those achieved by means of exchange transfusion or dialysis. This method has the added advantage of universal availability and ease of administration.

Prognosis and outcome varies not only with the toxicity of the product and the dose ingested but also with variation in the individual tolerance and susceptibility and with the difference in susceptibility in the same person at different times.

Home Visits by Public Health Nurse.—The value of a home visit by an experienced public health nurse cannot be overemphasized. It is vital in obtaining pertinent facts and data about the mode of occurrence, e. g., how the accident happened. The visit should be timely and will have great educational value, since it is made in relation to a recent accidental occurrence. The preventive aspect can be pinpointed and defined. The family will still be in a receptive frame of mind and can be easily motivated.

Of the families visited 78% were cooperative and pleasant. Information was given freely, and they were grateful for the interest and concern shown by the Poison Control Center. In addition to many accidental hazards existing in the home, other significant health problems were often noted such as acute illness, lack of supervision of well children, behavior problems, or lack of prenatal care for pregnancy in the second or third trimester. Referrals to appropriate treatment agencies were made in each case.

It may be of interest to mention that in New York City about 250,000 home visits are made annually by public health nurses for various health reasons. The nurses have become so sensitized to the accident prevention program that they utilize each visit to observe potential hazards and provide the needed safety education on corrective measures.

The role of the nurse is well illustrated by an actual case report which was received in the middle of May. The nurse visited the home because of a missed scheduled appontment at a child health station. She noticed a 20-month-old child who appeared very drowsy. The mother was in bed, recuperating from the effects of an incomplete abortion. The nurse elicited the following story.

An older sibling, 5 years of age, had given the patient a bottle containing 5-grain (0.325-Gm.) aspirin tablets, which he obtained in the kitchen, to play marbles with while he watched a television program. The infant ingested 15 tablets. This had happened on the day preceding the nurse's visit. The nurse urged immediate medical care which the mother refused, whereupon the nurse called the district health officer, who was very "persuasive." On admission to the hospital, over 24 hours after ingestion, the child presented the symptoms of nausea, vomiting, and stupor. The poisoning was severe and the patient was on the critical list for two days. He was given a transfusion of 500 cc. of whole blood, continuous intravenous administration of fluids for three days, and supportive therapy. After five days of hospitalization the child made a complete recovery. Since the mother did not appear in good health, the nurse referred her to a nearby gynecologic clinic. The family was also advised by the public health nurse to move the medicine cabinet from its present low level in the kitchen to a higher and less accessible place. Return visits to this home were also scheduled. The alertness and action of the nurse in this incident were most likely lifesaving.

Role of Poison Control Center.—Reassuring and allaying the anxieties of parents, physicians, and hospital personnel in minor "nontoxic" incidents and avoiding unnecessary overtreatment is one of the center's helpful functions and most rewarding roles. A gratifying example of this function occurred, also in the middle of May. The Newark (N. J.) Poison Control Center advised St. Barnabas Hospital in that city to call our center for information relating to a tarantula bite. A warehouse employee who was unloading bananas had been bitten by a tarantula which was hidden among the bananas. Happily, the center was able to provide immediately information that the size and fearsome appearance of the tarantula is not related to its mild toxicity. All concerned were relieved.

Comment

Our data indicate that children involved in accidental poisonings are not significantly different physically or mentally from the "average" child. Accidental ingestion was not a manifestation of retarded growth and development but was closely correlated with the age of the child, the accessibility of poisonous substances, socioeconomic conditions, and lack of direct adult supervision at time of occurrence.

The accident was due in the main to the interaction of an inexperienced, uncautious host, a potentially toxic agent, and an unsafe environment. This combination makes an accidental occurrence almost inevitable. Many of the families interviewed were unaware that the agents involved were hazardous, nor were they aware of the danger of practices employed in the storage and handling of products.

Other contributory factors were the removal of toxic substances from the original container and its transfer to a household utensil. The placing of containers of similar size, shape, and color and with similar labels adjacent to one another in medicine cabinets has inherent dangers and potential hazards. A mix-up in identity often follows. The evil practice of giving children handbags which contain medicaments to play with is also a frequent source of poisonings. The inadequate labeling of household products which contain toxic ingredients often has grave consequences.

The period of moving from one apartment to another is one of particularly high hazard potential. The normal supervision of even well-managed homes is subject to disorganization. The careless handling of "samples" by physicians in their homes and offices and of medicaments in hospitals is also a frequent cause of needless accidental poisonings.

Accidental chemical poisonings are of multiple etiology. Many of the causes, particularly the human factors involved, genetic and psychosocial, are still in the realm of the unknown. As a result of epidemiologic investigations, however, a considerable body of knowledge has been accumulated which, if put into immediate action, would materially aid in the prevention of poisonings.

Prevention Through Education

Education of the Profession.—The management and treatment of poisonings is an important responsibility of a Poison Control Center, and these have resulted in the saving of many lives and countless disabilities, an important facet of secondary prevention. The chief focus now, however, must be on primary prevention, the total prevention of accidental chemical poisonings. It is assumed that this can best be accomplished by means of reliable education effectively directed to all levels. One of the fundamental lacks, discovered by inquiries and reports received soon after the establishment of the center, was in further training of interns and residents in hospital practices in the management of poisonings and a careful and detailed scrutiny of existing hospital emergency room procedures. It was also felt by the Poison Control Center Technical Advisory Committee at its first meeting that education would be more effective if it began at the undergraduate level in all medical schools and schools of nursing and pharmacy. This program was soon put into effect, and the facilities of the center are now utilized for training purposes in nearly all medical schools and schools of nursing in the city. Field visits and didactic presentations are included.

An increasing number of requests are being received from many hospitals within the city and from nearby states for presentations at their scheduled monthly staff meetings. The ensuing discussion, with wide audience participation, is rewarding. Similar requests are being received from many committees of the local medical societies and branches of the American Academy of Pediatrics.

Education of the Public.—Our safety and accident prevention program, of which poison control is but one facet, is predicated on the assumption that education is the most potent weapon in the control and prevention of accidents. All mediums, the press, radio, and television, are effectively utilized. Outdoor advertising companies and transportation facilities have also provided free space for the display of signs and posters. Health education material is widely disseminated through the schools, clinics, child health stations, drugstores, and other services. PTA groups and health and welfare agencies are also involved.

It is gratifying to relate that interest in the Poison Control Program has increased in geometric progression. Unlike campaigns which have a tendency to reach a peak and then abate, the interest in the prevention of accidental chemical poisoning has become accelerated with renewed vigor and intensity.

In spite of the gains made, the full potential of public education has not yet been fully exploited. It requires the collective efforts of the entire community, physician, pharmacist, public health worker, nurse, hospital staff member, pharmacologist, engineer, industrialist, housing authority, law enforcement officer, social scientist, lawyer, psychiatrist, educator, and environmental sanitarian. Legislation relating to dosage, packaging, standardization, and proper labeling of poisonous substances is part of the educational program and should be used as an educational device and not merely as an enforcement procedure.[13]

There is still much to be deplored in the sales techniques and promotional efforts used by some pharmaceutical manufacturers. Exaggerated claims are often made without mention of side-reactions, treatment of overdoses, and precautionary measures to be employed in storage and handling. A continuing interest by health departments is needed in promulgating regulations designed to promote the safety of children. These should be evaluated to determine their effectiveness or need for modifications. While proper labeling of a toxic substance, as recommended by the A. M. A. Committee on Toxicology, is exceedingly important, sole reliance must not be placed on it, since many who are subject to accidental poisonings cannot read. Other safeguards must also be employed. Manufacturers of household products and pharmaceutical companies must carry on, in addition to their sales programs, an equally vigorous and effective educational safety campaign. They must also continuously seek to substitute nontoxic ingredients for hazardous ones and to design "safer" containers.

The educational program must be based on facts, accurate, reliable, devoid of overdramatization, simply told, and pinpointed to the vulnerable groups and the specific hazards.

Physician as Educator.—The physician, as a key member of the poison control team, can make a significant contribution in solving this problem. He has knowledge of the cultural, biological, physical, and social environment of the families he serves. He also knows the children's stage of growth and development and the habits and attitudes of the adult members of the household.

He must appoint himself as a one-man poison control center to his patients. His primary task should be to inform himself about the various hazards associated with drugs and household preparations, the epidemiology of poisonings, the dangers associated with improper storage and handling, and the population at highest risk in the same manner as he acquaints himself about diagnosis, therapy, and prevention of infectious and communicable diseases.

During home and office visits the physician can and should provide anticipatory guidance on the poisonings most likely to occur at a given age and stage of development and how to prevent them. His medical record should include a specific inquiry about poisonings in the patient and the family and their mode of occurrence.

The physician has an unparalleled opportunity, during home visits for whatever purpose, to observe possible existing hazards, to pinpoint them, and to advise and motivate the family to eliminate the existing hazards promptly. Unlike genetic or other biological factors the physical environment can easily be altered and made safer for children. Parents need, however, advice and counsel from a physician whom they respect about the importance of safer habits and attitudes and about the maintenance of safety precautions in and about the home. Considerable health education can and should be provided also during office visits. The physician's waiting room should include informative and reliable health education literature and visual aids on the occurrence and prevention of accidental chemical poisonings. A safety check list may also profitably be distributed to parents.

The greatest care should be observed when a medicament is prescribed. The quantity prescribed should be small, sufficient to meet only immediate needs. In addition to oral instructions, detailed, specific, legibly written instructions about the dosage, time interval, brand, and whether it is to be used for internal or external purposes should be left with an adult member of the family.

The instructions, both oral and written, should include strong emphasis on the need for keeping the medicament in the original container and also for keeping all drugs and preparations out of reach of children. "Samples" should best not be dispensed, but, if they are, extreme caution should be exercised that the container is legibly marked, i. e., with the type of medicament dispensed, its dosage, when it is to be taken, and warnings about safekeeping.

The physician should also inquire periodically whether his instructions are being followed. As a staff member of a hospital the physician should also observe any existing unsafe practices within the hospital where he serves, such as the dispensing of drugs in hospital pharmacies without appropriate identification data and without warning about safekeeping and whether drugs and preparations are within easy reach of children, and take the necessary countermeasures. The physician should also warn strongly against self-treatment.

I am in wholehearted agreement with the view, expressed in an editorial in THE JOURNAL,[14] that prescription labels should also bear the name of the drug and that this practice "would work for good rather than for harm." The plain designation of the principal ingredients on the prescription label would be of immeasurable help to poison control centers in many cases of poisonings and might even be at times lifesaving. To motivate others, the physician must himself assume safe habits and attitudes and scrupulously practice them at all times in his own total environment.

The physician should report to the local health department all poisonings, including side-reactions and overdoses. Since drug reactions are truly "poisonings," the term "side-reactions" is a convenient euphemism for poisonings. One of the additional developing functions of a poison control center is the accumulation of new knowledge and data relating to side-reactions, toxicity of new products, and iatrogenic accidents. Only by means of such studies will it be possible to determine whether a drug is safe for a specific use. The physician can aid greatly in the acquisition of such knowledge by prompt reporting of such incidents to the poison control center. Any previously unknown hazard should be immediately reported by physicians so that it may be widely publicized and the public properly alerted, such as was the case with the dangers associated with the plastic bag.

Summary

This study is based on 23,862 accidental poisonings (those from gas excluded) reported to the New York City Poison Control Center from March 10, 1955, to the end of December, 1958. Of all poisonings 54.7% occurred in persons under 20 years of age.

Children under 5 years of age, who constitute only 8% of the total population, accounted for 46.2% of all poisonings. Of the 13,069 poisonings reported in persons under 20 years of age 84.4% occurred in children under 5 years of age. The high incidence at these ages is related to a lack of adequate supervision, availability, careless handling and storing of drugs, and lack of caution and experience.

Internally taken drugs caused nearly 50% of all poisonings, with barbiturates and aspirin as the chief offenders. Next in frequency were poisonings due to household preparations, followed by those with externally applied drugs and cosmetics, pesticides, and miscellaneous products such as lead.

The higher incidence noted in certain ethnic groups was most likely due to their low socioeconomic status and not to any inherent differences. No significant sex difference was observed.

Five leading toxic agents were responsible for 30% of all poisonings in persons under 20 years of age. Children involved in poisonings were not dissimilar from the average in growth and development, physical or mental. A definite correlation, however, was found with socioeconomic conditions, availability and accessibility of poisonous substances, and age.

Nearly all poisonings are preventable. The most important item in prevention is knowledge and information about the risk involved and the population at risk. Regulations and labeling alone will not prevent accidental poisonings but must be coupled with education. Socioeconomic conditions, culture, ignorance, customs, and traditions profoundly influence occurrences. A full understanding of the dynamics of accident causation is a prerequisite to the formulation of sound countermeasures. Only sound intensive epidemiologic and other research studies will provide the necessary clues and guideposts for a successful attack on this major public health problem. There is still a wide gap, however, between available knowledge and its application. Immediate action is needed to close this gap. Further delay is unwarranted.

Prevention is possible through education at all levels. Education requires an integrated team approach with the family physician as key member of the team. Accident prevention, of which poison control is only one aspect, merits the greater attention and involvement of the practicing physician.

Suggestions of value to this study were made by Mr. Harry W. Raybin, technical director of the Poison Control Center.

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MANAGEMENT OF THE PATIENT WHO FAILS TO VOID AFTER OPERATION

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Postoperative overdistention of the bladder should be avoided, but this does not justify leaving routine postoperative catheterization orders to the interpretation and discretion of the nursing service. If the attending physician, intern, or nurse gives adequate attention to the patient during the first few hours after an operation, the frequency of catheterizations can be greatly reduced. Responses to a questionnaire sent to 111 physicians of the American Urological Association indicated that catheterization is usually not considered necessary during the first six hours and thereafter is necessary only if the patient has not urinated voluntarily and has a full bladder. The attending physician should evaluate the need for catheterization and should, whenever possible, perform it himself. When catheterization is done without a break in the sterile technique and with caution to avoid tissue damage, complications are infrequent.

It has been disturbing to me, during the last few years, to observe the increasing lack of respect for and the often unconcerned, indiscriminate use of the catheter by both medical and nursing staff. This situation exists largely because of increased numbers of patients hospitalized and decreased numbers of trained professional help. Lest we forget the many complications that may follow the "sinking of the catheter," it would be well to organize our thoughts on the subject.

The use of the term "postoperative urinary retention" here is confined to those patients unable to void after operation in spite of a full bladder, normal kidney function, and the absence of organic obstruction. Experience is a great teacher, when accepted in proper spirit; however, too often we are willing to accept only our own and fail to appreciate the intelligent experience of others. Even Hippocrates was not that naïve. He knew that experience was deceptive. Something else was requisite, a philosophical orientation or, as it was later termed, "logos harnessed to a method."

Changing trends exist in hospitals today with regard to patient care. Personal attention to patients' simple wants and needs is often lacking. It is thought to be somewhat "old-fashioned" to request that a considerate attitude be displayed. For example, many patients could urinate spontaneously after operation if the urinal were present and within reach. Adequate personal preoperative and postoperative instruction to the patient lends confidence and mental tranquillity of a degree far superior to that effected by tranquilizing agents. It has been shown that personal preoperative and postoperative discussions and suggestions with 2,000 patients lowered the percentage of those who had to be catheterized from 18.3 to 1.7.[1]

Throughout the years in a good many hospitals it has become customary for the trained orderly to catheterize a male patient. The operation of passing a soft rubber catheter is not difficult for one who is experienced and versed in sterile technique. I have no thought of being critical of this program, but this is not the point in question. I question not the actual act but rather, "Is this procedure really necessary?" The answer to this can come only from the doctor in charge, his associate, or his assistant. Consideration must be given to the extent of the surgical procedure, the patient's state of hydration, whether or not gastrointestinal suction has been employed, and, finally, the state of all vital signs, with particular attention to blood pressure levels adequate for glomerular filtration.

A somewhat similar situation exists with regard to catheterization of the female patient. The present curriculum of student nurse training leaves a great deal to be desired. Real bedside nursing has also become "old-fashioned" and is for practical purposes a "lost art." Many tasks, including catheterization, are relegated to nonprofessional nursing help, and the new graduate soon finds she has much to learn before she can become a good nurse.

The chief mistake that many physicians make is the manner in which postoperative catheterization orders are written. The order to catheterize every 6, 8, or 12 hours or "prn if unable to void" is totally unrealistic. The patient may have a full bladder in 2 hours or only 150 cc. in 12 hours. Here again, personal supervision by the doctor is necessary in the best interests of the patient's postoperative care.

Catheterization of the bladder is not without danger. Despite the most careful technique, infection of the bladder may follow. Overdistention injures the bladder and the injured tissue makes an ideal culture medium, as was pointed out long ago by Cabot. Previous experimental work has shown that bacteria may be transferred from the urethra into the bladder during passage of the

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Comment

With a mean monthly rate of secondary failure of response to tolbutamide of 3% of patients in a three-year follow-up, it is obvious that half of the good results will become secondary failures every two years. Thus, if one starts with 100 patients who respond to administration of tolbutamide, there will be 50 under treatment after 2 years, 25 under treatment after 4 years, 12 under treatment after 6 years, 6 under treatment after 8 years, and 3 under treatment after 10 years. Perhaps this dismal prognosis can be improved by more careful selection of the patients started on this treatment. Our data do not suggest how this selection can be made (see table). Unresponsiveness to tolbutamide is usually permanent, regardless of whether it is a primary or secondary failure. Occasionally, a temporary response is obtained after a period of insulin therapy, but this transient response is usually inadequate and requires administration of large doses of tolbutamide. Chlorpropamide and metahexamide have been recommended for the treatment of patients experiencing secondary failure of response to tolbutamide[4] and elicit a beneficial response in 20% of these patients. This response is often poor, however, and requires administration of large doses of the drug, with a definite, increased risk of liver damage. Because of the increased toxicity of the newer drugs their use should be restricted to the patient who has failed to respond to adequate doses of tolbutamide (3 Gm. per day) and a low-calorie diet.[5] The higher incidence of beneficial effect reported in the literature may be due to the fact that it is easier for a patient to remember to take 4 chlorpropamide tablets each morning than it is for the patient taking tolbutamide to remember to take 3 tablets twice each day.

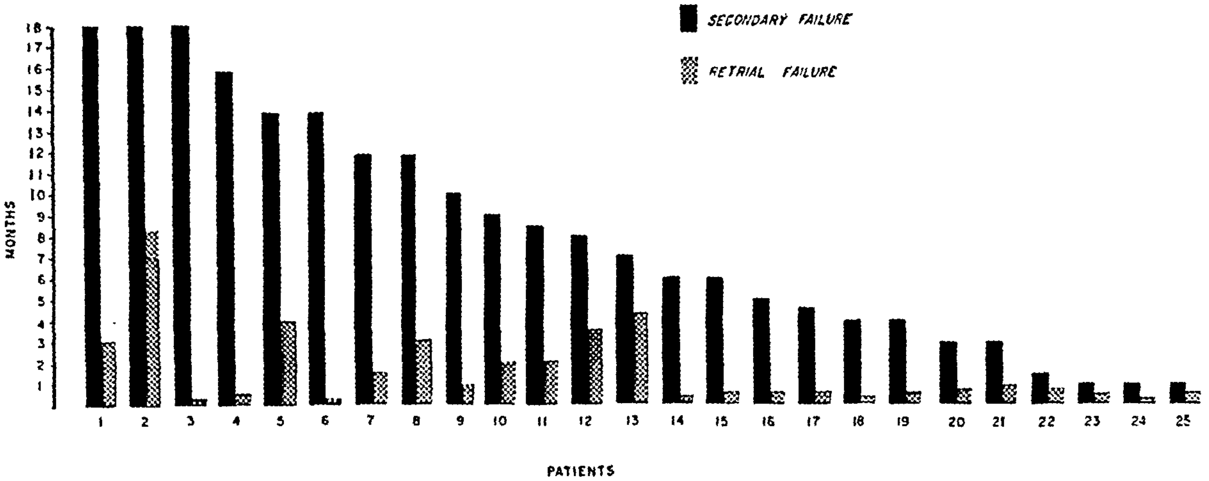

Fig. 8.—Duration of satisfactory response in patients given retrial on tolbutamide subsequent to rest period after secondary failure.

Some may doubt the advisability of giving a drug whose effect is so temporary to a group of patients who have a life-long disease. We have never seen harm come from the administration of tolbutamide. Those patients who are spared insulin injections for even a few months are grateful for this reprieve. Therefore, we follow the policy of giving sulfonylurea drugs to all of our new nonketotic, mature diabetics when their diabetes cannot be controlled by simple caloric restriction.

Summary and Conclusions

The significant findings of a follow-up study of nonketotic diabetic patients treated with tolbutamide (Orinase) are as follows: 1. In a group of 200 patients who received tolbutamide and were followed up for up to three years the rate of secondary failure of response to the drug was 29.5%. In the first year the rate of failure in the same group of patients had been 16%. The monthly rate of secondary failure averages about 3% of the patients treated each month. If this rate continues, all patients will eventually become resistant to the hypoglycemic effects of tolbutamide. 2. Patients with poor and fair initial diabetic control develop secondary failure sooner than those with good and excellent control. 3. There was no significant

TABLE.—*Characteristics of Patients Aiding in Prediction of Response to Administration of Sulfonylurea Drugs*

Characteristics	Satisfactory Response	Secondary Failure	Primary Failure
Age at onset	Over 40 yr.	Near 40 yr.	Under 40 yr.
Duration of diabetes	Newly diagnosed	Less than 3 yr.	Over 3 yr.
Previous treatment	None	Small dose of insulin	Large Dose of insulin
History of acidosis	No	Rare	Often
Symptoms of diabetes	Minimal or none	Mild to moderate	Severe classic
Weight	Slight obesity	Normal or marked obesity	Underweight

change in the insulin requirements of patients before treatment with tolbutamide and after their secondary failure of response to the drug. 4. Only 2 of the 25 patients who were given a retrial on tolbutamide therapy obtained a good response. Therefore, it can be anticipated that once a patient fails to respond to the drug the failure will be permanent. 5. A satisfactory response to treatment with chlorpropamide (Diabinese) or metahexamide (Euglycin) was obtained in 20% of the patients in whom secondary failure of response to tolbutamide had occurred. Phenethylbiguanide (DBI) gave a satisfactory response in 55% of these. 6. All mature, nonketotic diabetics whose condition cannot be controlled by diet alone deserve a trial on tolbutamide therapy. 7. These patients must be followed up at least every two months, because they may develop secondary failure with little warning and no apparent cause.

3805 Florence Dr., Alexandria, Va. (Dr. Moss).

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PRACTICAL HINTS IN THE EARLY DIAGNOSIS OF MULTIPLE SCLEROSIS

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It has been stated statistically that the average case of multiple sclerosis is diagnosed five years after the onset of the disease.[1] It is the purpose of this paper to set forth a few practical hints that may alert the general practitioner or internist that multiple sclerosis, in a mild form, may be the cause of a patient's complaints. These complaints may, at first, be a single presentation such as one of the neuritides and later, or after careful neurological examination, a multiplicity of defects are noted and the diagnosis becomes apparent.

It is common knowledge, from the standpoint of pathology, that multiple sclerosis is a "patchy" type of demyelinating disease. It usually involves the central nervous system in a "hit-or-miss" pattern and is likened to syphilis, which can imitate any disease.[2] I have found clinically, however, that certain signs and symptoms of multiple sclerosis seem to be more prominent than one would expect from a "hit-or-miss" pattern.

Etiologically, the disease is obscure, but certain evidence lately, especially from British workers,[3] seems to indicate that there is an initial episode of sore throat or upper respiratory infection followed by a sensitization and aseptic inflammation of parts of the central nervous system. This type of mechanism operates in rheumatic fever, in which the myocardium and valves are the shock organs, and in acute glomerular nephritis, in which the shock organ is the kidney.[4]

Suppose then, for a moment, we accept the above hypothesis, and a patient is treated by his physician for an acute respiratory infection. This patient appears at the office two or three weeks later and complains of numbness or weakness of an arm or a leg, of a hemicrania in the area of the eye, or of visual blurring; we as physicians are apt to dismiss the episode with a wave of the arm—"neuritis, myositis, or sinusitis"—and treatment in the form of B vitamins is usually prescribed. This last episode could be the initial onslaught of multiple sclerosis in certain susceptible persons. A careful follow-up examination, especially if the symptoms recur, may reveal changes in reflexes or some muscular atrophy or weakness.

Symptoms Which May Be Overlooked

The Neurotic.—The neurotic patient with a multiplicity of complaints (such as aches, pains, numbness of extremities, extreme fatigue, weakness, inability to cope with everyday chores, and vertigo) for some unknown reason is particularly susceptible to multiple sclerosis. Usually the patient has visited every physician within a radius of 50 miles and always receives the same knowing smile, a pat on the back, and a prescription for phenobarbital, or, in tune with the latest fad, one of the tranquilizers. A carefully taken history, however, may reveal a multiplicity of neurological complaints and a careful neurological examination may reveal changes sufficient to warrant a guarded diagnosis of possible multiple sclerosis.

Optic Neuritis.—Adie states that 34% of all cases of optic neuritis progress to multiple sclerosis.[5] Recently statistics collected after World War II indicate that the majority of cases of optic neuritis progress to some type of demyelinating disease and that of this group 60% develop multiple sclerosis. Beware of the patient with optic neuritis, especially if there is no toxic chemical reason for the disease.

Pregnancy.—Pregnancy is considered to be a stress state both mentally and physically. Opinion is divided as to the influence of pregnancy on multiple sclerosis. Some physicians believe there is no clear-cut evidence that the disease is adversely affected by pregnancy; on the other hand, some feel that the chance of a severe exacerbation is so great that normal pregnancies are interrupted to prevent relapses.[6] Merritt states that frequently early signs and symptoms of multiple sclerosis appear during pregnancy. I have observed 3 cases in 16 (19%) recently surveyed[7] in which multiple sclerosis first developed during pregnancy. It is interesting to note that in another case, during a routine prenatal physical examination, a positive Babínski sign on the left with 0.5-in. atrophy of the gastrocnemius muscle was revealed. This patient developed cranial nerve malfunctions, chiefly confined to the olfactory tract, and a mild left-sided hemiplegia during the postpartum period. She has been examined carefully in a large teaching hospital and multiple sclerosis has been found to be the cause of her trouble. Recently she has been examined again by me and an almost complete remission has been effected. This remission, it is believed, has been accomplished with use of six whole-blood transfusions[8] plus ACTH therapy.[9]

In my opinion, all physicians who practice obstetrics should include a careful neurological examination as part of their general physical examination in order to uncover mild or incipient multiple sclerosis.

Dizziness and Vertigo.—As with optic neuritis, a transient episode of dizziness and vertigo after remission may progress to a multiplicity of neurological complaints that may be a clue in the early diagnosis of multiple sclerosis. These patients are usually placed on bed rest and given the usual sedatives that affect the middle ear. The end-result is recovery in spite of the drugs. Later after careful evaluation there may be an arm or leg that does not function in its usual manner. The progression of these symptoms makes follow-up examination and neurological evaluation mandatory.

Trifacial Neuralgia.—Trifacial neuralgia seems to come and go in some persons for no apparent reason. This type of symptom always makes me suspicious, because in my limited experience the only neurological disease known to me that progresses and regresses for no apparent reason is multiple sclerosis. It is apparent again that with the above history a careful appraisal of other parts of the central nervous system should be carried out—not once or twice but periodically, if this disease is to be identified.

In one patient who was observed this presenting symptom progressed to numbness and poor maneuverability of the right arm and hand. Later the patient developed bladder weakness, and after careful study she was believed to have multiple sclerosis.

Ataxia.—Hysterical ataxia is quite common, but at least this symptom is dramatic enough to warrant further examination. In two patients I have observed one was given the diagnosis of hysteria and the other of a residual effect of poliomyelitis. Both patients later developed dysfunction of the urinary bladder and cranial nerve palsies. Both later, after elaborate analyses, were believed to have multiple sclerosis.

Obvious Neuromuscular Defects.—A group of neuromuscular defects are so obviously due to disorders of the central nervous system that a glance at the patient determines that further appraisal and referral is necessary. These include scanning speech, gross nystagmus, gross intention tremor, obvious dragging of a leg or a wasted arm, and dysarthric and marked gait difficulties. These defects are not the prime interest of this paper but rather the insidious, mild, and transient attacks which escape detection unless the physician is alerted to the possibility of prodromal multiple sclerosis and a careful follow-up examination is performed periodically. I have found it particularly helpful to ask the patient to telephone immediately and report any new symptoms or variations of old symptoms noted at the office. This technique has revealed pathological reflexes which were not present one week to 10 days later.

Summary

It is suspected that there is a fairly common mild type of multiple sclerosis (usually in allergic persons) that is transient in nature and difficult to diagnose because of a single presentation of symptoms. On careful neurological examination and periodic follow-up other central nervous system areas are noted to become involved and the diagnosis gradually becomes obvious. These persons are

predominately young (aged 20 to 40 years) and are predominately female. They are usually labeled as neurotics and their definitive diagnosis is not usually uncovered until five years after their symptoms have started. Cranial nerve palsies usually usher in mild attacks and are followed later by other disabilities of the central nervous system. Pregnancy, as a stress state, is unusually fertile ground in which to complete a careful neurological examination to uncover these mild cases. Immediate examination of new developments because of their transient nature is imperative to clarify the diagnosis.

Cedar Street.

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RELATIONSHIP OF PERIODIC MENTAL STRESS TO SERUM LIPOPROTEIN AND CHOLESTEROL LEVELS

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Blood samples obtained from medical students during an initial period of moderate stress were compared with samples obtained during more stressful examination periods with respect to serum lipoprotein and total serum cholesterol levels. An atherogenic index (AI) was calculated to represent two classes of lipoproteins determined by ultracentrifugation. In one group of 37 students the serum cholesterol level rose from an initial mean value of 191 to one of 235 mg. per 100 ml., and the AI rose from an initial value of 45 to one of 57. Similar results were found in a second group of 13 students. The increase in AI was due to a greater than 50% increase in the lower density lipoprotein fraction. It is suggested that this fraction may be the factor that relates stress to atherosclerosis and coronary artery disease.

Many environmental factors are presently being studied in order to ascertain their relationship to the atherosclerotic process. The roles of nutrition, sex, heredity, hormonal imbalance, and exercise are among those being studied most intensively at the present time. The high incidence of diseases resulting from atherosclerosis among business executives and others under constant pressure has led many persons to speculate that emotional stress may be yet another important factor in atherogenesis; only recently, however, has there been any acceptable evidence to support this concept. Friedman and co-workers[1] reported increases in serum cholesterol levels and decreases in blood clotting times in men subjected to cyclic variations of occupational stress. Several authors have found that serum cholesterol levels are elevated in students during periodic mental stress associated with examination schedules.[2] The mechanism of this increase in serum cholesterol levels under mental stress remains unexplained. In an attempt to further understand the changes in

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serum lipid levels under stress we have studied the effects of comprehensive final examinations on the levels of different serum lipoprotein classes, as well as on serum cholesterol levels, in medical students.

Methods and Materials

Serum lipoprotein and total serum cholesterol values were determined in groups of sophomore and freshman medical students. Blood samples were taken from a group of 37 male sophomore students during the middle of the winter academic quarter. Samples were again taken from the same students during final examinations at the end of this quarter. Comprehensive final examinations were given at the end of the quarter and no other examinations were given to the students during the quarter. This same procedure was repeated on a group of 13 freshman medical students during the middle of the spring quarter and again at examination time. Blood samples were all collected in the postabsorptive state. Serum lipoproteins were analyzed in a Spinco Model E Analytical Ultracentrifuge by the method of Lindgren and co-workers[3] and De Lalla and co-workers.[4] The standard Svedberg flotation unit (S_f) 0-12 and 12-400 lipoprotein classes and the atherogenic index of Gofman[5] were determined. The atherogenic index (AI) is calculated in the following manner:

$$AI = \frac{(\text{standard } S_f \text{ 0-12}) + 1.75\ (\text{standard } S_f \text{ 12-400})}{10}$$

where standard S_f 0-12 and 12-400 values are in milligrams per 100 ml. and the factor of 10 in the denominator is arbitrary, being used to achieve a convenient scale of AI values. The total serum cholesterol levels were determined by the method of Pearson and co-workers.[6]

Changes in Serum Lipoprotein and Cholesterol Levels During Examination Periods

Sophomore Students

Period	No. of Students	Mean Cholesterol Value and Standard Error of Mean, Mg.%	Standard S_f 0-12 Class Level and Standard Error of Mean, Mg.%	Mean Standard S_f 12-400 Class Level and Standard Error of Mean, Mg.%	Atherogenic Index
Control	37	191±2.7	248±9.7	115± 9.7	45
Examination	37	235±3.8	266±9.8	174±11.1	57
% Increase		23	7	51	26
Significance (p value)		<0.001	<0.3	<0.001	

Freshman Students

Period	No. of Students	Mean Cholesterol Value, Mg.%	Mean Standard S_f 0-12 Class Level, Mg.%	Mean Standard S_f 12-400 Class Level, Mg.%	Atherogenic Index
Control	13	190	225	109	42
Examination	13	241	203	170	50
% Increase		27	—10	56	19

Results

The table shows the changes in serum lipoprotein and serum cholesterol levels during examination periods for both sophomore and freshman students. Results for both groups show markedly similar changes. Serum cholesterol levels showed a 23 and 27% increase during comprehensive final examinations for the sophomore and freshman students respectively. The standard S_f 0-12 class increased only 7% in the sophomore students while the same lipoprotein class showed a 10% decrease among the freshman students at examination time. The standard S_f 12-400 class increased 51 and 56% and the atherogenic index increased 26 and 19%, respectively, in the two groups during examinations. Among the sophomore students 14 of the 37 (38%) had a greater than 50 mg.% increase and 26 of the 37 (70%) had more than a 25 mg.% increase in cholesterol levels at examinations. In the same group 10 of the 37 (27%) had an increase of greater than 100 mg.% in the standard S_f 12-400 class, and 23 (62%) of the group showed an increase of greater than 50 mg.% in the same lipoprotein class. Seven of this group showed no change or a decrease in the standard S_f 12-400 class.

Comment

The findings of this study support those of previous work which indicated that serum cholesterol levels are increased during mental stress. The sophomore class studied in this paper had been previously studied for changes in cholesterol levels during examination periods as compared to control periods. As we have already reported,[2a] this group showed increases in serum cholesterol levels of 16.5 and 11.0% during final examinations of the winter and spring quarters of the previous year. The present increase of 23% is the third consecutive significant elevation in serum cholesterol levels during periodic mental stress for this class of students.

From the present data it would appear that the changes in serum lipids during mental stress are limited primarily to the S_f 12-400 class of lipoproteins. Both groups of students studied here showed a greater than 50% increase in this fraction during examinations, without significant changes in the S_f 0-12 class.

The significance of elevated lipoprotein and cholesterol levels in the development of atherosclerosis is not well understood at the present time.

However, studies in experimental animals,[7] patients with coronary artery disease,[8] and populations in which extensive atherosclerosis is common[9] suggest that elevated lipid levels play some role in the production of this disease. Any factor which leads to the presence of higher serum lipid levels should be worth considering as a possible factor in atherogenesis.

Evidence is rapidly accumulating which suggests that emotional stress is one such factor leading to elevated lipid levels. The mechanism of this increase is not apparent at the present time. According to Friedman and associates[10] increases in cholesterol values during occupational stress cannot be explained on the basis of dietary changes. Apparently this elevation is limited to the lipids of the lower density lipoprotein molecules (S_f 12-400 class). It is of interest to note that Gofman[5] found increased levels of this lipoprotein class to have a higher statistical correlation to the occurrence of coronary artery disease than those of any other lipoprotein class.

Summary

A group of 37 sophomore medical students and one of 13 freshman medical students were studied to determine the effects of examination schedules on serum lipoprotein and cholesterol levels. During examinations the cholesterol levels increased 23 and 27% over control periods of relative relaxation for the two groups respectively. The changes in standard Svedberg flotation unit (S_f) 0-12 lipoprotein classes were not significant, but the standard S_f 12-400 classes increased 51 and 56% for the two groups. The mechanism for the increase in the low-density S_f 12-400 lipoprotein class is not apparent at the present time, but it is interesting to note that Gofman[5] found increased levels of this lipoprotein class to have a higher statistical relationship to the occurrence of coronary artery disease than those of any other lipoprotein class.

This study was supported by the Houston Heart Association.

Technical assistance was furnished by Roger M. Sebbane.

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SPORTS AND SPORTS INJURIES.—To many people sports means competitive sport, and the development of the outstanding athlete. . . . Let us not forget, however, the large number of sport participants who fail to reach top standard. Their efforts are not wasted, and their work is just as important. The greatest value of sport is in raising the general standard of physical and mental health in the community. . . . It becomes important to pay due attention to the prevention and treatment of sport injuries. Some sports have hazards peculiar to themselves—e.g., brain damage in boxers, head injuries in cyclists, fractured legs in skiing. The treatment of sports injuries is peculiarly difficult because of the tendency, particularly in competitive sport, to return to activity before recovery is complete. The pressure for such premature resumption of sporting activity comes not only from the athlete himself, but even from the club, and must be resisted at all costs. Such premature resumption of activity before recovery is complete only leads to further trouble and prolonged disability, which is harmful, not only to the athlete, but to the club itself. It should be realized that it never pays to play unfit men.—L. T. Wedlick, Sports Injuries, *The Medical Journal of Australia*, June 13, 1959.

SUPERIOR VENA CAVA–RIGHT MAIN PULMONARY ARTERY ANASTOMOSIS

SURGICAL CORRECTION FOR PATIENTS WITH EBSTEIN'S ANOMALY AND FOR CONGENITAL HYPOPLASTIC RIGHT VENTRICLE

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Ebstein's anomaly and congenital hypoplasia of the right ventricle give rise to signs and symptoms of partial obstruction to outflow from the right atrium, and this may lead to right heart failure. Successful surgical correction or relief of these defects has not been previously reported. Anastomoses between the superior vena cava and the right pulmonary artery have been established in a 4-year-old girl with congenital hypoplasia of the right ventricle and in two patients, aged 8 and 14 years, with Ebstein's anomaly. Relief of the distention and of the elevated pressure in the right atrium was immediately apparent in these three patients. The 14-year-old girl died four days after operation, and autopsy revealed a thrombosis of the left main pulmonary artery, but the two patients aged 4 and 8 years continued to show marked clinical improvement. The desirability of eventual closure of the septal defect remains to be decided.

Partial obstruction to right atrial outflow due to an inadequate right ventricular filling capacity is common to Ebstein's anomaly and to hypoplasia of the right ventricle. A successful surgical correction or relief of this type of obstruction has not been previously reported. The following case is reported to illustrate the salient features of the hemodynamics in these anomalies and to demonstrate the surgical treatment by which an appreciable degree of improvement may be obtained in this group of patients.

Report of a Case

A 2-year-old female child with a known heart murmur since birth was first admitted to the hospital on May 16, 1957. There was a history of swelling of the feet and of the abdomen of two weeks' duration and of occasional cough and nocturnal dyspnea for one month prior to admission. Physical examination revealed that the patient was thin and in marked respiratory difficulty. Ascites and pitting edema of the extremities were present, as well as moderate cyanosis of the lips and nailbeds. The neck veins were slightly distended. Subcostal retraction was present on inspiration. The temperature was 100.2 F (37.9 C) and the pulse rate was 118 per minute and regular. Blood pressures were 96/60 mm. Hg and 100/58 mm. Hg in the right arm and left leg respectively. The cardiac apex was palpable at the sixth left intercostal space in the anterior axillary line. The first heart sound was normal and heard best at the apex. The second heart sound was normal and closely split and was maximal at the second left intercostal space. A third heart sound was heard along the left sternal border. No significant murmur was heard. The phonocardiogram (fig. 1) confirmed the above auscultatory findings and revealed a late diastolic deflection of low amplitude and frequency along the left sternal border, maximal at the fourth left intercostal space. The sound that we had interpreted as a third heart sound was thus shown to be a fourth heart sound due to atrial contraction. The liver was palpable 8 cm. below the right costal margin. The hemoglobin level was 8.5 Gm. per 100 ml., the erythrocyte count was 3,100,000 per cubic millimeter, and the leukocyte count was 8,350 per cubic millimeter with a normal differential count. The urinalysis revealed normal findings.

The electrocardiogram (fig. 2) demonstrated a sinus rhythm with a rate of 115 per minute. The electrical position of the heart was horizontal and the standard limb leads showed an electrical axis of −15 degrees. The P waves were tall and peaked in leads 1, 2, aVF, V_2, and V_3, with an amplitude of 4.5 mm. in lead 2. The S wave measured 19 mm. in V_2 and the R waves measured 26 mm. in V_6. This electrocardiogram was interpreted as showing right atrial and left ventricular hypertrophy.

Roentgenograms (fig. 3 *A* and *B*) of the chest demonstrated probable right atrial and left ventricular enlargement. There was no evidence of left atrial enlargement, and pulmonary vascular markings appeared to be within normal limits.

Biplane venous angiocardiograms taken at 8 films per second on the Elema apparatus demonstrated a large right atrium and a small right ventricle. The

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pulmonary artery appeared to be normal in size but the concentration of contrast substance in the peripheral pulmonary vessels was diminished.

Right heart catheterization (see table) done on June 14, 1957, demonstrated normal pressures in the right ventricle and pulmonary artery. The pressure contour of the right ventricle and the pulmonary artery had a narrow ejection peak. There was an elevation of the end diastolic pressure due to transmission of the prominent "a" wave from the right atrium (fig. 4). The right atrial mean pressure was normal but a tall "a" wave was present which measured 7 mm. Hg. The left atrium was entered repeatedly. The pressure-pulse in this chamber was identical with that of the right atrium in both height and contour. The blood sample collected from the left atrium was normally saturated, but a review of all the data suggested that this sample was obtained from a pulmonary vein. An arterial oxygen saturation of 83.9% was obtained from the femoral artery two days later and was incorporated into the catheterization data for calculation of flows and shunts. The left-to-right shunt was 0.51 liters per minute per square meter of body surface and the right-to-left shunt 4.87 liters per minute per square meter of body surface. A series of spot films taken with the guidance of pressure recordings while the catheter was being withdrawn from the right ventricle to the right atrium appeared to demonstrate the normal location of the tricuspid valve. The catheterization data were interpreted as demonstrating an interatrial septal defect with a predominant right-to-left shunt in the presence of normal right ventricular pressure. These findings, along with electrocardiographic evidence of right atrial hypertrophy, phonocardiographic demonstration of a constant fourth heart sound, and right atrial and left ventricular enlargement shown on chest roentgenograms and angiocardiograms, were considered to be indicative of Ebstein's anomaly, with a bidirectional but predominantly right-to-left shunt at the atrial level. Although patients with left ventricular hypertrophy have been reported, with the diagnosis verified at autopsy, the absence of bundle-branch block and the failure to demonstrate definite malposition of the tricuspid valve made the above diagnosis doubtful. The evidence of congestive heart failure disappeared promptly (fig. 3) with a regimen of oxygen, digitoxin, ammonium chloride, and antibiotics, and the patient was discharged markedly improved on July 3, 1957.

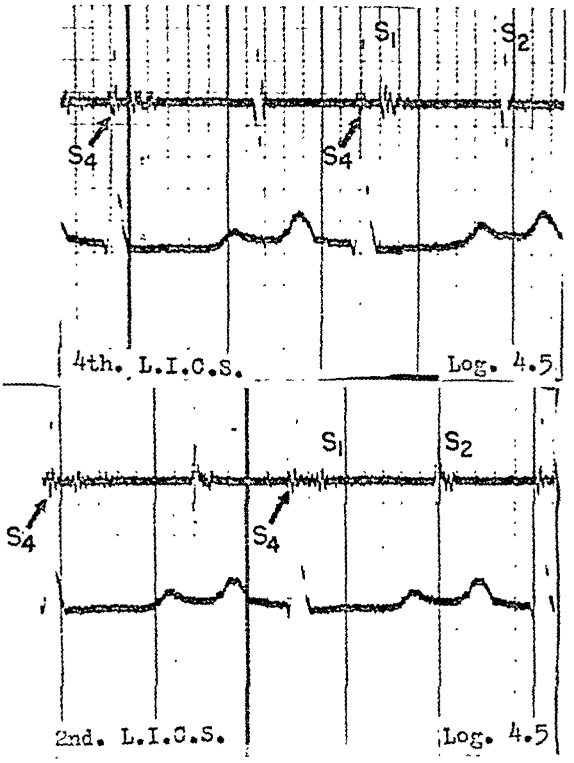

Fig. 1.—Phonocardiogram taken on first admission, showing a fourth heart sound. S_1—first heart sound, S_2—second heart sound, S_4—fourth heart sound, L. I. C. S.—left intercostal space.

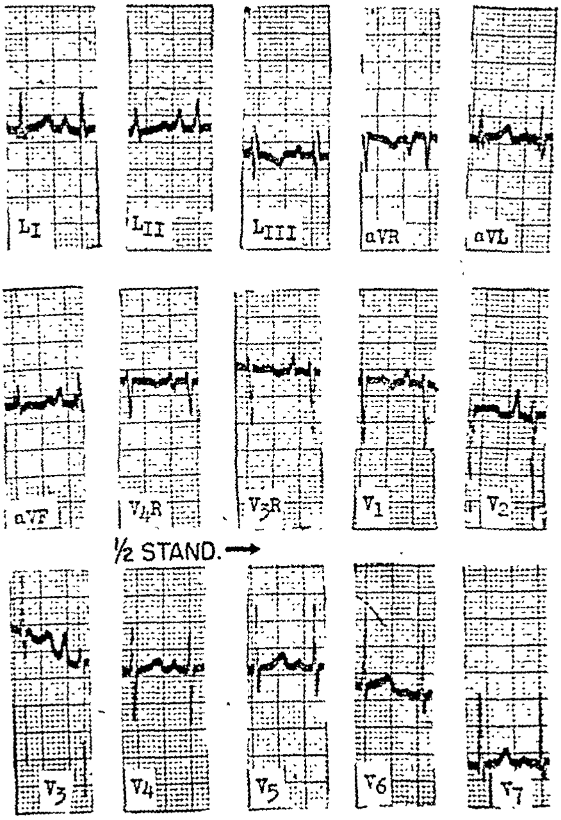

Fig. 2.—Electrocardiogram taken on first admission, showing left axis deviation, right atrial enlargement, and left ventricular hypertrophy.

The patient was lost to follow-up for two years and did not return to the hospital again until March 26, 1959, when she was admitted to the general pediatric ward for treatment of an upper respiratory infection. After two weeks of therapy with antibiotics, she was transferred to the pediatric cardiology department. Physical examination again revealed cyanosis of the lips and nailbeds and clubbing of the fingers and toes. The temperature, respirations, and pulse rate were normal. Blood pressures in the right arm and left leg were 90/60 mm. Hg and 110/80 mm. Hg respectively. The apical impulse was palpable at the fifth left intercostal space in the midclavicular line and was hyperdynamic in character, suggesting the presence of left ventricular hypertrophy. The first heart sound was normal and maximal at the apex. The second heart sound was normally split. As on the previous admission, a constant fourth heart sound was heard along the left sternal border. A short systolic ejection murmur was heard at the left sternal border, maximal at the second and third intercostal spaces. These auscultatory findings were confirmed by phonocardiography. The blood and urine examinations were again within normal range. The 15-lead electrocardiogram and the roentgenograms again demonstrated right atrial and left ventricular enlargement.

Two biplane angiocardiograms were performed on the Elema apparatus at 8 films per second. The first was done by injection of the contrast substance into the left ventricle through a catheter advanced into this chamber from the right atrium through an interatrial septal defect. It demonstrated a large left ventricle and a somewhat dilated aorta. There was no evidence of a shunt at the ventricular level. The second angiocardiogram was done by injecting the contrast substance through a catheter placed in the right atrium (fig. 5). These films demonstrated a large right atrium and a small right ventricular cavity. The pulmonary artery appeared slightly decreased in size and the peripheral pulmonary vascular markings were diminished. There was immediate opacification of the left atrium and the left ventricle through the right atrium.

The second cardiac catheterization (see table) was done on May 6, 1959. The pressure-pulse contour of the right ventricle again demonstrated a narrow ejection peak and transmission of the "a" wave in late diastole. The right atrial mean pressure was elevated, measuring 7 mm. Hg, and the pressure pulse contour was still dominated by a tall "a" wave measuring 8 mm. Hg. A slight pressure gradient of 2 mm. Hg was present across the tricuspid valve. The tricuspid valve was thought to be normally located. The pressure-pulse contour of the left atrium was identical with that of the right atrium. There was an elevation in oxygen content of more than 1 vol.% in the blood samples obtained from the right ventricle and the pulmonary artery as compared with the mixed venous samples. One

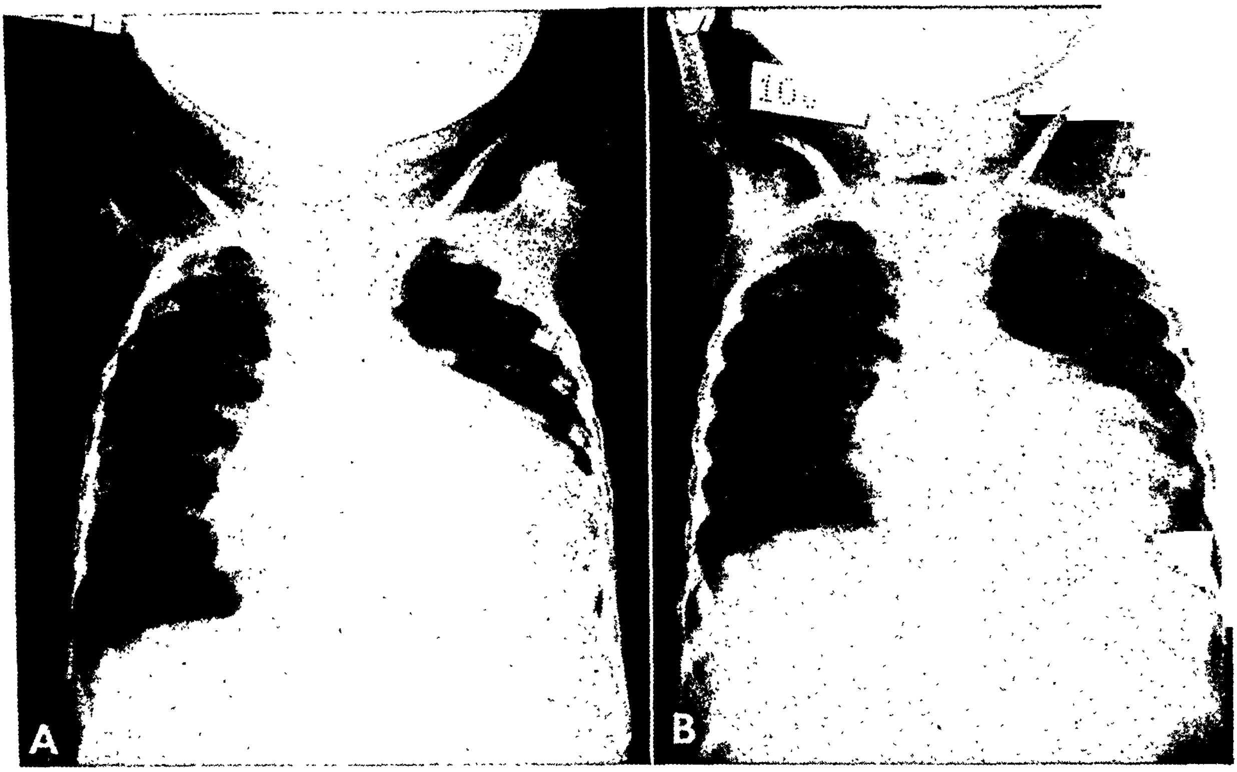

Fig. 3.—Roentgenogram of chest: *A*, posteroanterior view of chest taken on first admission (May 16, 1957), demonstrating cardiomegaly with evidence of right atrial and left ventricular enlargement. *B*, posteroanterior view of chest on May 29, 1957, after treatment for congestive heart failure.

sample obtained from the right atrium again showed marked elevation in oxygen content. Blood samples obtained from the left atrium, left ventricle, and femoral artery were similar in oxygen content, with saturations of 75.9, 79.2, and 80.6% respectively. The close approximation of oxygen contents confirmed the presence of a right-to-left shunt at the atrial level. The repeated demonstration of restriction to right ventricular filling again suggested a diagnosis of Ebstein's anomaly. However, the failure to demonstrate malposition of the tricuspid valve made a diagnosis of congenital tricuspid stenosis seem a more likely possibility. The absence of a marked diastolic gradient could be explained on the basis of right atrial decompression through an interatrial septal defect.

Results of Cardiac Catheterizations

Oxygen Analyses

Location	June 14, 1957 Oxygen Content, Vol. %	June 14, 1957 Saturation, %	May 6, 1959 Oxygen Content, Vol. %	May 6, 1959 Saturation, %
Inferior vena cava	13.35		11.46	
Superior vena cava	12.79		10.26	
Upper right atrium	12.92		10.85	
Middle right atrium			14.40‡	
Lower right atrium	17.90†		11.61	
Right ventricular inflow	13.99		11.94	
Right ventricular mid	14.19		12.51	
Right ventricular outflow	13.98		12.89	
Main pulmonary artery	14.21		12.31	
Left pulmonary artery			12.90	
Pulmonary vein	19.11	98.9		
Left atrium			13.69	79.5
Left ventricle			13.62	79.2
Left femoral artery	Clotted		13.88	80.6
	(Oxygen capacity 19.33)		(Oxygen capacity 17.21)	
Left femoral artery, two days later	18.55	83.9		
	(Oxygen capacity 22.11)			

Intravascular Pressures

Location	Mm. Hg	Mm. Hg
Right atrium (mean)	(3)	(7)
"a" wave	7	8
"v" wave	4	4
Left atrium (mean)	(3)	(7)
"a" wave	7	8
"v" wave	4	4
Right ventricular inflow	25/4	22/5
Right ventricular outflow	19/5	21/5
Main pulmonary artery	21/9	19/10
Left pulmonary artery		19/10
Pulmonary capillary (mean)	(3)	(7)
Left femoral artery	97/52	

Flows and Shunts

	Liters/Min./Sq. M.	Liters/Min./Sq. M.
Pulmonary blood flow	3.14	4.25
Systemic blood flow*	4.87	5.02
Left-to-right shunt	0.51	1.20
Right-to-left shunt	2.24	1.97

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*Systemic blood flow and right-to-left shunt calculated with use of presumed peripheral oxygen unsaturation of 83.9%, as manifested by femoral arterial saturation performed two days later.

†Lower right atrium sample might be collected in or near left atrium.

‡Sample might be collected close to left atrium or pulmonary vein.

Surgical Procedures

On June 19, 1959, surgical exploration was carried out. The heart and great vessels were exposed through a median sternotomy. The heart was moderately enlarged, and the right atrium was seen to be markedly distended. Pressure curves recorded from the right atrium and right ventricle by direct puncture were similar in contour and amplitude to those of the second cardiac catherization. Digital exploration through the right atrial appendage confirmed the presence of a 3-to-4-cm. defect in the inferior portion of the atrial septum. There was no evidence of tricuspid stenosis, and the tricuspid valve was thought to be in its normal position. The capacity of the right ventricle was found by one of us (E. H. F.) to be markedly reduced, with the walls unusually smooth and lacking the normal papillary musculature. The exploring finger could be passed from the right atrium into the pulmonary artery without encountering an obstruction other than the reduced cavity of the right ventricle. Evaluation of the clinical and hemodynamic findings with those at the operating table led us to assume that, if a portion of the blood returning to the heart could be diverted directly into the pulmonary artery, pressure in the right atrium would be reduced, with a resultant decrease in the right-to-left shunt. It appeared to us that this could be accomplished by anastomosis of the superior vena cava to the right main pulmonary artery, a procedure that had been previously successfully performed for patients with tetralogy of Fallot and tricuspid atresia. However, the midsternal incision precluded this type of operation at that time. The wound was therefore closed and the patient was returned to the recovery room and made an uneventful recovery.

On July 17, 1959, the child was returned to the operating room and the heart and great vessels were exposed by right anterolateral thoracotomy in the fourth intercostal space. After appropriate dissection to expose the superior vena cava and the right main pulmonary artery, these two vessels were divided close to their origin and an end-to-end anastomosis was carried out between the distal segments of the superior vena cava and the right main pulmonary artery. The segments were closed with suture ligatures. The total time of occlusion of the superior vena cava was 12 minutes and was tolerated well by the patient. Relief of the distention of the right atrium was immediately apparent. Pressure recordings were taken at the operating table after completion of anastomosis (fig. 6, *top*). The mean pressure in the right atrium was zero, with disappearance of the prominent "a" wave. The pressure-pulse contour in the right ventricle no longer showed the end-diastolic elevation or the narrow ejection peak. It was decided that it was preferable to leave the atrial septal defect open to serve as a site for continued decompression of the right atrium.

The child made an uneventful recovery. The temperature became normal after the second postoperative day. When the patient was last examined on Aug. 3, 1959, the temperature, pulse, and respiration were normal. The cardiac apex was in the fifth left intercostal space just outside the midclavicular line. The first heart sound was normally split maximal at the apex. The second heart sound was also split maximal at the second left intercostal space. The fourth heart sound could no longer be heard and could not be identified on the phonocardiogram. There was a short systolic ejection murmur at the second left intercostal space. The posteroanterior view of the heart on the roentgenogram revealed a definite decrease in the convexity of the right heart border indicating a smaller right atrium. The electrocardiogram showed a definite decrease in amplitude of P waves (fig. 6, *bottom*). The peripheral arterial oxygen saturation obtained from the femoral artery was 85.9%, an increase of 6%. The patient will have angiocardiography and right heart catheterization within the next three months.

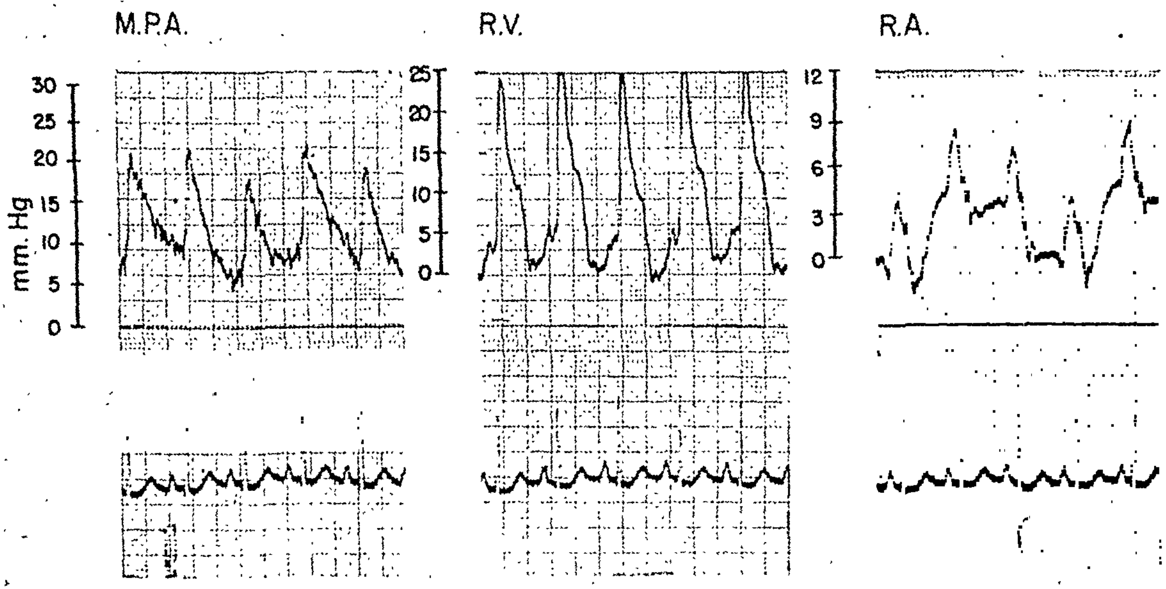

Fig. 4.—Pressure-pulse recorded during first cardiac catheterization, demonstrating narrow ejection peak in pulmonary artery and right ventricle, transmission of "a" into right ventricular pressure curve, and tall "a" wave in right atrial tracing.

Comment

The diagnostic features of Ebstein's anomaly have been well documented in the excellent reports of Blount and associates,[1] Mayer and co-workers,[2] and others.[3] Isolated hypoplasia of the right ventricle is an extremely rare anomaly.[4] The hemodynamic responses in the two entities appear to be identical, with limitation of right ventricular filling creating a resistance to emptying of the right atrium. This resistance is reflected by an increase in the mean right atrial pressure, resulting in dilatation and hypertrophy of the atrium. In the majority of the patients, cardiac output becomes inadequate to meet the demands of growth and activity, and cardiac failure or fatal arrhythmia occur in childhood and early adult life. Most of the patients develop cyanosis eventually. If an atrial septal defect or patent foramen ovale is present, cyanosis may be evident during infancy. In those patients without an interatrial communication, cyanosis may develop on the basis of congestive heart failure, with excessive reduction of oxyhemoglobin at the capillary level.

The hemodynamic changes are well demonstrated by clinical and physiological studies. Dilatation of the right atrium may be demonstrated by the roentgenogram of the chest and angiocardiograms. Hypertrophy of the right atrium is reflected in the increased amplitude of the P waves and suggested by a constant fourth heart sound. Cardiac catheterization usually reveals an elevation of mean pressure in the right atrium and, if the tricuspid valve is competent, accentuation of the right atrial "a" wave, indicating contraction of the hypertrophied atrium against resistance to right ventricular filling. As in the case presented in this report, the prominent "a" wave may be transmitted to the right ventricular pressure curve. When tricuspid insufficiency accompanies Ebstein's anomaly, the elevated "a" wave is not seen and the "v" wave of the atrial pressure curve may be markedly accentuated.

Attempts to achieve correction or palliation in Ebstein's anomaly have been unrewarding. Wright and associates [5] reported subjective improvement in one patient in whom the atrial septal defect was closed, but subsequent patients died after the same procedure. Several attempts have been made to reattach the tricuspid valve to its normal position, but to our knowledge no patient has survived this procedure.[6] The reported cases of Ebstein's anomaly in which subclavian-pulmonary artery anastomoses have been done have all ended fatally. Successful superior vena cava–right main pulmonary artery anastomoses have been reported in patients and in laboratory animals.[7] An excellent laboratory investigation of the procedure, with hemodynamic studies, has been reported by Robicsek and associates.[8] We have performed this procedure in two infants with tricuspid atresia. The first infant, 3 months of age, died shortly after the operation with signs of superior vena cava obstruction. It is likely that the very small vessels in a child of this age made this patient a dubious choice for a venous anastomosis. The second child, 9 months of age at the time of operation, has done quite well. Postoperative angiocardiography in this patient demonstrated the patent anastomosis with excellent concentration of the contrast substance in the pulmonary vessels of the right lung.

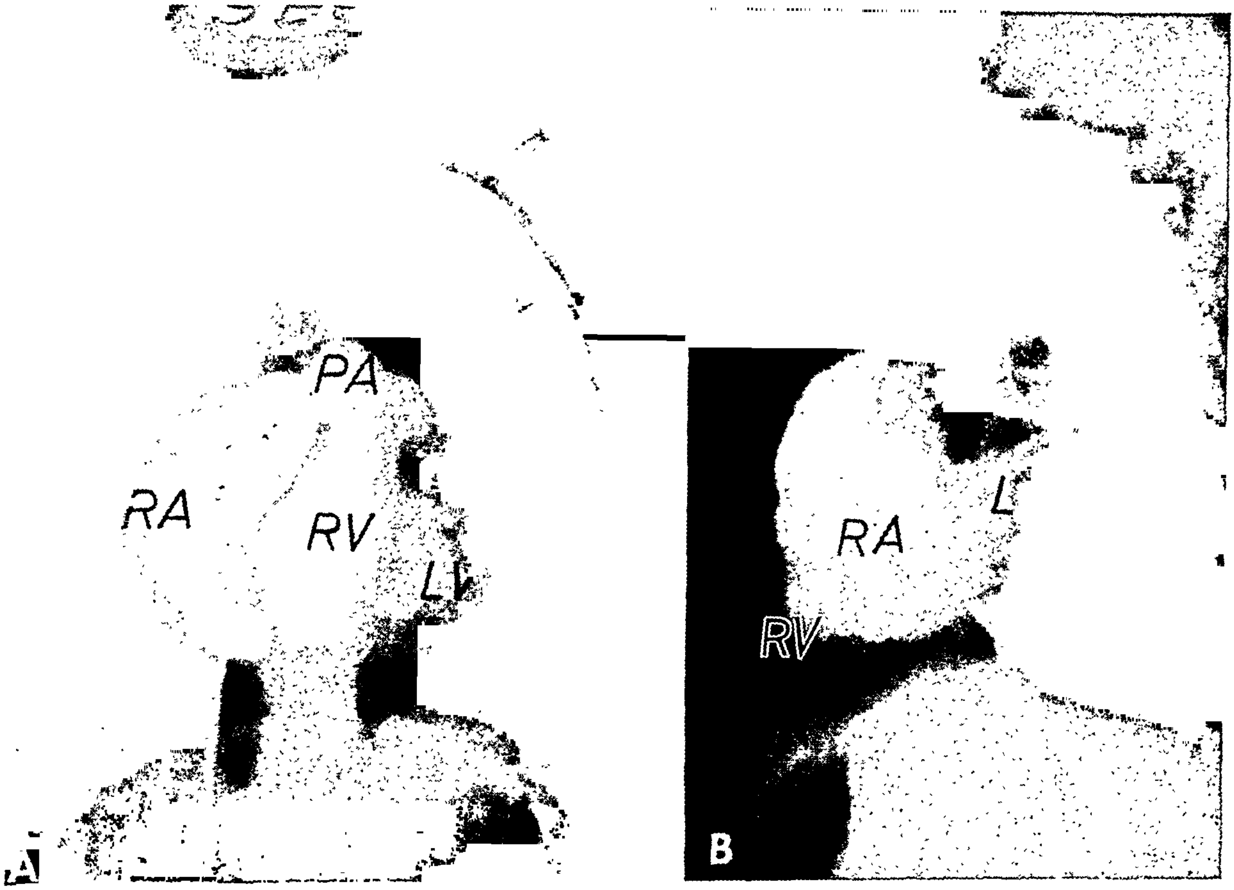

Fig. 5.—Second selective angiocardiogram performed during second admission, demonstrating large right atrium, small right ventricular cavity, and pulmonary artery with decreased peripheral pulmonary vascular markings. There was also early opacification of left ventricle. RA—right atrium, RV—right ventricle, LV—left ventricle, PA—pulmonary artery.

We were unable to find any case report in the literature of the superior vena cava–right pulmonary artery anastomosis in patients with Ebstein's anomaly or hypoplastic right ventricle, but we wish to give credit to Glenn [7a] for being the first to point out the possibility of performing this procedure in patients with the above-mentioned entities.

It appears to us that the shunting of blood flow from the superior vena cava directly into the pulmonary artery is particularly applicable to Ebstein's anomaly and to hypoplasia of the right ventricle, and the physiological data presented, as well as the child's clinical improvement, tend to confirm this opinion. The diversion of approximately 40% of the venous return to the heart away from the right atrium is a definitive measure by which overdistention and increased pressure in this chamber may be relieved, and direction of the blood into the pulmonary artery assures its adequate oxygenation. The desirability of closure of the atrial septal defect after performance of the anastomosis will require further study. The pressures taken at the operating table showing normal values represent the relationships of resting cardiac output. It was our opinion in this case that the defect should be left open to allow decompression of the right atrium, if that becomes necessary for the increased cardiac output demanded by growth and activity.

The performance of the superior vena cava–right main pulmonary anastomosis is not difficult for an experienced vascular surgeon. The details of the operative procedure have been adequately described by Bakulev and Kolesnikov.[9] The obvious objections involve the possibility of clotting in a venous anastomosis and, when an end-to-end anastomosis is done, the necessity for temporary occlusion of the superior vena cava. Neither of these objections has proved serious in the reported cases or in our limited experience except in the infant with tricuspid atresia with a very small pulmonary artery.

Considerable caution should be, and is intended to be, exercised in suggesting the use of a palliative operation on the basis of an experience with a single case. However, the application of a superior vena cava–right main pulmonary artery anastomosis in patients with Ebstein's anomaly or hypoplasia of the right ventricle appears to be physiologically sound, and the expectation of early death in unrelieved severe cases should justify its trial.

Summary

A superior vena cava–right main pulmonary artery anastomosis has been performed for palliation in a 4-year-old cyanotic child with a limited right ventricular filling capacity and a right-to-left shunt through an atrial septal defect. The clinical and physiological data supported a diagnosis of Ebstein's anomaly in this child, although malposition of the tricuspid valve could not be demonstrated; an isolated hypoplasia of the right ventricle was also a possible diagnosis. In either case the hemodynamic responses are identical, with a partial obstruction to right atrial emptying resulting in an increase in pressure in the right atrium; dilatation and hypertrophy of the right atrium; a right-to-left shunt if an atrial septal defect is present; and eventual heart failure. Shunting of the superior vena cava directly into the main pulmonary artery resulted, in the case presented, in marked clinical improvement, relief of cyanosis, and lowering of right atrial pressure to a normal level. It is suggested that this operative procedure has a sound physiological basis for significant palliation in patients with Ebstein's anomaly or hypoplasia of the right ventricle.

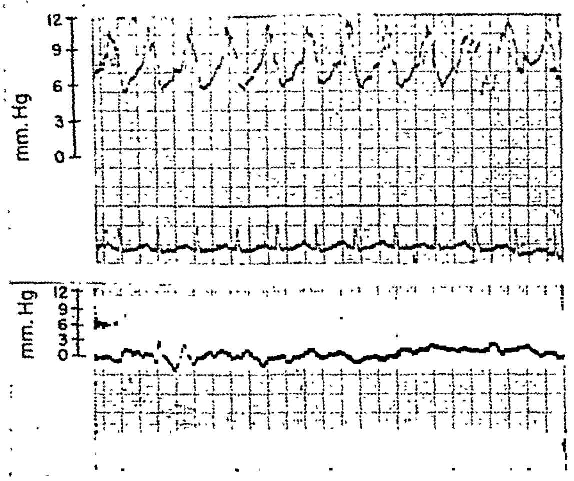

Fig. 6.—Intravascular pressure recordings during surgery before (*top*) and after (*bottom*) superior vena cava–right main pulmonary artery anastomosis, with open chest, demonstrating a drop of right atrial pressure of 8 mm. Hg and disappearance of tall "a" wave.

Addendum

Since the report of the above case, two patients, 14 and 8 years of age, with clinical, roentgenographic, electrocardiographic, angiocardiographic and cardiac catheterization evidence of Ebstein's anomaly, were operated on on July 29, 1959, and July 30, 1959, respectively, with superior vena cava–right main pulmonary artery anastomosis. In both cases there was a decrease in right atrial pressure immediately after surgery. There was marked clinical improvement in the 8-year-old child. The 14-year-old patient showed a decrease of peripheral cyanosis until the fourth postoperative day, when her clinical course deteriorated rapidly and she died because of propagation of a thrombus from the proximal stump of the right main pulmonary artery into the left main pulmonary artery.

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RESTORATION OF GASTRODUODENAL CONTINUITY

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The feasibility of reoperating to restore gastrointestinal continuity was studied in 30 patients who had suffered disabling complications after gastroenterostomy. The largest group consisted of 13 patients in whom the original operation was vagotomy and gastrojejunostomy. All of the 30 patients had symptoms so severe as to prevent them from carrying on gainful occupations, and in each case medical treatment had been given a thorough trial. The corrective operation consisted of closing the gastrojejunal stoma and frequently included end-to-end anastomosis for repair of the jejunum and end-to-end anastomosis between stomach and duodenum. Only one patient failed to obtain relief by the corrective operation; eight others were but partially relieved and required continued medical or dietary treatment. Twenty-one became free of symptoms, were relieved of the need for medication, and were able to return to work.

One of the serious problems arising from the surgical treatment of duodenal ulcer is the malfunctioning of the gastrojejunal stoma after simple gastrojejunostomy or gastric resection of the Billroth 2 type.

This presentation deals with 30 patients who suffered disabling complications arising from both types of operations and the surgical measures used in attempts to correct the disturbances encountered. No cases of marginal ulcer are included in this group. These constitute what we consider to be a separate entity, and they have been dealt with by other types of surgical treatment.

In 13 of the 30 patients the original operation was vagotomy and gastrojejunostomy; in 10 the original operation was gastrojejunostomy alone; and in 7 the original operation was gastric resection of the Billroth 2 type. In all of the patients the reason for surgical treatment was benign peptic ulceration of the duodenum or stomach. There were 28 males and 2 females in the group. The preponderance of males is probably explained by the fact that the study was conducted in a veterans' hospital. The patients' ages ranged from 30 to 66 years, with an average age of 46 years.

The problem of disabling digestive symptoms after operations for the treatment of peptic ulcer which bypass the duodenum has been recognized for some years. As early as 1935, Perman[1] described disabling effects of Billroth 2 procedures in three patients, and recently Perman and others[2] have published reports of the favorable effects of converting a Billroth 2 to a Billroth 1 operation for the relief of the disability.

These patients were disabled by their postoperative symptoms to a degree that prevented them from carrying on gainful occupations or otherwise enjoying normal activities. All were more uncomfortable and disabled than they were before the primary operation; pain was the prominent symptom in 73%, nausea and vomiting in 56%, the "dumping syndrome" in 50%, bleeding in 30%, and diarrhea in 20%; weight loss occurred in 53% of the group (see table).

Before they were referred to the surgical service for restoration of the normal continuity of the stomach and intestine, all of the 30 patients were studied and given a thorough trial of medical treatment. Analysis of the gastric secretions showed the acidity within normal range in 43%, hypoacidity in 40%, and hyperacidity in 17%. X-ray examinations of the stomach and intestine were interpreted as showing functioning gastrojejunal anastomosis in all patients. In no case was there evident of gastric retention. Stomal ulceration was not demonstrated preoperatively. A few of the patients showed evidence of rapid emptying of the stomach. Gastroscopy was performed in 26 of the 30 patients and showed evidence of gastritis in most of them. Hemorrhagic gastritis was observed in 26%, atrophic gastritis in 7%, hypertrophic gastritis in 3%, and a mixed type in 33%.

At the time of corrective surgical intervention, all but one of the patients showed evidence of gastritis in the immediate proximity of the gastrojejunal stoma. The stoma was considered to be excessively large in several of the cases. In some, the jejunum was thickened and enlarged in its circumference in the 30 to 60 cm. immediately distal to the stoma. The change was suggestive of true hypertrophy.

The corrective operation in the patients with a Billroth 2 resection consisted of taking down the anastomosis between the jejunum and the stomach and reestablishing gastrointestinal continuity by an end-to-end anastomosis between the stomach and the duodenum (see figure). The corrective procedure in these patients in whom the original operation was gastrojejunostomy consisted of taking down the gastrojejunostomy and performing a

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From the Veterans Administration Hospital.

vagotomy and pyloroplasty of the Heineke-Mikulicz type (see figure). Repair of the jejunum after the take-down was by end-to-end anastomosis. An end-to-end anastomosis between the stomach and the duodenum was technically feasible in all the patients with a Billroth 2 resection. There were no operative deaths and no serious postoperative complications.

Results of Restoration of Gastroduodenal Continuity in Thirty Patients After Original Gastrojejunostomy or Billroth 2 Gastric Resection

Signs and Symptoms After Original Operation	Patients		Patients Relieved Postoperatively	
	No.	%	No.	%
Pain				
Severe	14	46		
Distress	8	27		
	22	73	18	82
Nausea and vomiting	17	56	16	94
Weight loss	16	53	12	75
Dumping syndrome	15	50	15	100
Bleeding	9	30	9	100
Diarrhea	6	20	6	100

Results

Postoperative relief of signs and symptoms of the 30 patients discussed in this report is indicated in the table. The progress of 28 patients was followed for periods ranging from six months to eight years, the average approaching six years. Eighty per cent were followed up for more than three years. The results were tabulated from questionnaires and personal interviews conducted by the writers.

Seventy-one per cent of the patients were completely relieved of disturbing symptoms. Seventy-eight per cent are on an unrestricted diet, and only 36% have found it advisable to take some form of medicament. Eighty-nine per cent were able to return to a gainful occupation, and the remaining 11% are retired.

None of the patients is unemployed because of a return of former symptoms or the development of new symptoms. There was a weight gain in 43%, and 46% have been able to maintain their weights. Only 11% lost weight after the corrective surgical treatment.

The results are classified as "good" in patients who are asymptomatic, eating a normal diet, not taking medicaments, and able to work and who express satisfaction with the procedure; 71% are in this group.

The results are classified as "fair" in patients who are partially relieved and able to work, but are taking some form of medicament or are on a restricted diet, even though they are satisfied with the end-results; 25% are in this group.

The "poor" results are in patients whose symptoms are unchanged and who are dissatisfied with the results. One patient (4%) is in this group.

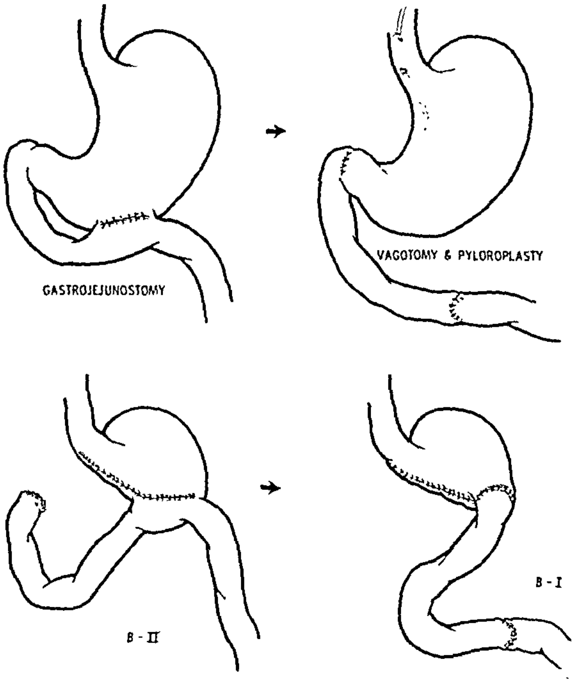
Comment

The patients comprising this series were severely ill with their symptoms. Schindler[3] has stated: "The symptoms of the diseased postoperative stomach are more difficult to influence than those of the original disease." Our experience supports his statement.

There is no unanimity of opinion regarding the pathophysiological changes responsible for the disabling symptoms. It is our opinion that regurgitation of intestinal juices into the stomach creates a type of gastritis which is refractory to medical management and that it is this mechanism which is chiefly responsible for the disability in the patients complaining of pain and bleeding.

It appears that the gastric mucosa has little resistance to the irritating effects of the intestinal juices. Palmer[4] made a study of 45 patients in whom the gastric mucosa was found to be normal prior to a surgical alteration which permitted a reflux of intestinal juices into the stomach. Biopsies of the fundic mucosa performed postoperatively on 22 of these patients showed evidence of gastritis.

Schindler[3] has carefully studied gastrojejunal stomas gastroscopically and has made interesting observations which lead him to believe that in cases in which no rhythmic stomal action is seen, reflux of intestinal juices produces gastritis.



Corrective restoration of gastroduodenal continuity.

Our studies indicate that the restoration of the normal continuity of the gastrointestinal tract by corrective surgery benefits the patient by relieving him of the pain of gastritis and by allowing the stages of digestion to proceed in an orderly manner, ingested food being exposed to the duodenal, pancreatic, and biliary juices after the food leaves the stomach.

Summary

Reestablishment of gastroduodenal continuity was done for 30 patients with disabling complications arising from a malfunctioning gastrojejunal stoma after simple gastrojejunostomy or gastric resection of the Billroth 2 type. Good results were reported in 71%, fair in 25%, and poor in 4%.

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PHEOCHROMOCYTOMA IN PREGNANCY

REPORT OF A FATAL REACTION TO PHENTOLAMINE (REGITINE) METHANESULFONATE

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Pheochromocytoma occurring simultaneously with pregnancy is not common. If suspected, it deserves every diagnostic effort because the death rate in patients with the combination is 50%. Hypertension and other symptoms caused by the tumor may be mistakenly ascribed to toxemia of pregnancy. The early prenatal course of a 21-year-old woman was normal except for occasional headaches in the fifth month. In the sixth she complained of some dizziness. Albuminuria and blood pressure levels of 130/80 to 160/100 mm. Hg were not controlled by the usual management of preeclampsia. Phentolamine methanesulfonate was given to test the suspected presence of a pheochromocytoma. Immediately after it was administered, the patient developed profound vasomotor shock and the baby and mother died. A pheochromocytoma was found in the left adrenal gland at autopsy.

Since the first report of the clinical picture of pheochromocytoma in 1922 by Lance and co-workers [1] about 300 cases have been recorded. Of about 175,000 annual deaths due to hypertension it has been estimated that 800 are due to pheochromocytomas.[2] Graham [2a] estimated that pheochromocytomas cause 0.5% of the hypertension in the United States, in citing Smithwich's and his own figures of 1,700 surgical patients with hypertension. To the time of writing 35 cases of pregnancy complicated by pheochromocytomas have been recorded.[3] The combination of pheochromocytoma and pregnancy is quite lethal, as shown by a 45% maternal mortality reported by Peelen and DeGroat [3c] and a 50% maternal mortality as reported by Dean.[3a] Other authors, however, have reported the case of a woman with three successful pregnancies complicated by a pheochromocytoma which was diagnosed as preeclampsia in each instance. Since the undiscovered tumor has a poor prognosis and is amenable to definitive treatment surgically, the presence of this tumor should be sought diligently when suspected. By far the greatest number of recorded cases of pheochromocytoma have occurred in the last decade, undoubtedly because of not only the availability of diagnostic aids but also the increased awareness of this tumor among clinicians.

The following case report may aid in future management of these patients.

Report of a Case

A 21-year-old woman, para 0, gravida 2, was first seen Nov. 8, 1957. Her last menstrual period started June 12, 1957, and was normal. She complained of occasional moderate frontal headaches of one month's duration, which were relieved by aspirin and not accompanied by scotoma, tinnitus, or dizziness. Her estimated date of confinement was March 20, 1958.

She had been hospitalized during April, 1957, for multiple small densities of her lungs which were not found to be actively tuberculous. She discharged herself against medical advice and apparently did well. Her family history was free of known hypertension, renal disease, tuberculosis, or cardiovascular disease. Two family members were asthmatic, a living sister and her deceased mother. Her father and two other siblings were living and apparently in good health.

On examination she was an asthenic, well-nourished, moderately developed woman in no distress. The blood pressure was 130/80 mm. Hg, pulse 120 per minute and regular, height 5 feet 3 in. (160 cm.), and weight 98½ lb. (44.7 kg.). The height of the uterine fundus was 15 cm. above the symphysis pubis. The hemoglobin level was 12 Gm. per 100 cc. Result of the Kahn test was negative. The blood was type O, Rh-negative. The urine showed a trace of sugar but was negative for albumin and blood cells. At the next monthly visit, Dec. 10, 1957, the blood pressure was 140/100 mm. Hg, the pulse 104 per minute and regular, and she weighed 103 lb. (46.8 kg.). She continued to complain of frontal headaches, which had not increased in severity or frequency, and some slight, intermittent dizziness. Because of the elevated blood pressure she was placed on therapy with phenobarbital and a low-sodium diet.

In spite of a program of phenobarbital, low-sodium diet, bed rest, intramuscular and oral administration of reserpine (Serpasil), promazine (Sparine), amisometradine (Rolicton), prochlorperazine (Compazine), and hydralazine (Apresoline) hydrochloride, her blood pressure rose, accompanied by increased severity of the frontal throbbing headaches and dizziness. Because of the refractoriness of her condition and the appearance of a retinal hemorrhage in the right eye she was admitted to the hospital on Dec. 27, 1957, with the diagnosis of atypical toxemia. The highest single blood pressure reading was 160/120 mm. Hg during her outpatient course, and biweekly urinalyses were negative for albumin, sugar, and blood cells.

Hospital Course.—On admission the blood pressure was 174/100 mm. Hg, the pulse 78 per minute and regular, the temperature 98 F (36.7 C), and the respiratory rate 22 per minute and regular. She was asthenic, anxious, apprehensive, and in a moderate amount of acute distress. Examination revealed a uterine size compatible with 6½-month gestation. Admission laboratory studies revealed catheterized urine containing a trace of albumin, trace of sugar, and occasional white blood cells, with specific gravity 1.015; hemoglobin concentration 10 Gm. per 100 cc.; white blood cell count 17,400 per cubic millimeter, with 81% neutrophils; fasting blood sugar level 83 mg. per 100 cc.; and nonprotein nitrogen level 36 mg. per 100 cc. The admission chest x-ray was unremarkable.

She was placed on a program of heavy sedation with phenobarbital, promazine, and reserpine and strict bed rest, to which she responded well and became normotensive. However, when her medication was decreased her blood pressure promptly rose. Because of the nature of this "atypical toxemia," and the inability to control her hypertension with usual doses of hypotensive medicaments, obstetric consultation was obtained and the diagnosis of pheochromocytoma was entertained. At no time throughout her outpatient or hospital course did the patient show peripheral edema or have abdominal pain, nausea, or vomiting.

On Jan. 6, 1958, at 12:45 a. m. a phentolamine test was performed after all hypotensive medication had been withheld for a 14-hour period prior to the test. As precautionary measures an intravenous drip was started with 5% dextrose and water and about 1 mg. of phentolamine (Regitine) methanesulfonate was dropped in the right conjunctival sac to determine possible sensitivity. Result of the conjunctival test was negative at 15 minutes. At the onset of the test the patient was in a recumbent position and in a resting, quiescent but not basal state; the blood pressure was 180/110 mm. Hg, with a regular pulse of 84 per minute. Four milligrams of phentolamine methanesulfonate was given intravenously through the tubing over a 30 to 45-second period. The blood pressure immediately and precipitously fell to 0/0 mm. Hg and the patient complained of nausea, had a sensation of sinking, heard music, and stated that she felt as if she were going to die. She became pale, cool, and clammy, and her pulse was imperceptible. While shock measures were being taken the heart revealed a grossly irregular rhythm, with coupling of the heart sounds. About 1 mg. of levarterenol (Levophed) was injected slowly into the tubing of the intravenous drip, with the blood pressure returning within 30 to 45 seconds to 200/102 mm. Hg, with an irregular pulse of 160 per minute. Because of the subsequent progressive fall of the blood pressure, an intravenous infusion was begun, containing 2 mg. of levarterenol per liter of 5% dextrose in water. About one hour after the infusion was started the blood pressure rose momentarily to 220/140, after which it fluctuated around 130/100 mm. Hg, with a grossly irregular pulse of 148 per minute.

The levarterenol solution was maintained throughout the day; however, the rate of administration had to be progressively increased to maintain the blood pressure at normotensive levels. She was alert, talking, cooperative, oriented, and without signs of paralysis or sensory defect. Her cardinal symptoms were marked apprehension and temporary headaches with transient dyspnea when the levarterenol solution was administered too rapidly. An electrocardiogram made seven hours after the phentolamine test showed a ventricular rate of 150, with a sinus rhythm. The electrical axis was 0 degrees with a P-R interval of 0.09 seconds and QRS interval of 0.08 seconds. There was RS-T segment depression in leads 2, 3, aVF, and V_1; also tall pointed T waves in leads 2, 3, V_2, V_3, and aVF.

Because it had become necessary to administer the levarterenol solution at an excessive rate, and because of some deterioration of the patient's condition, the solution was changed so that each 1,000 cc. of 5% dextrose in water contained 4 mg. of levarterenol and 1 mg. of histamine base, which was added in hopes of stimulating the tumor to secrete endogenous pressor substances. This change was made at 9 p. m., at which time catheterization produced 120 cc. of normal urine. During the evening the patient had six episodes of emesis of coffee-ground vomit.

By the next morning she had become mildly stuporous, and at 3 a. m. Cheyne-Stokes respiration began. Catheterization at 4 a. m. produced 200 cc. of urine, giving a 24-hour urinary output of 670 cc. despite the intravenous administration of 6,500 cc. of fluid. She developed water intoxication, as manifested by profuse sweating, vomiting, cardiac arrhythmia, and mild edema of the hands and face. At 4:30 a. m. the blood pressure was unobtainable and she was comatose. The levarterenol solution had become progressively more concentrated so that at the time the blood pressure was lost each 1,000 cc. of infusion contained 12 mg. of levarterenol and 2 mg. of histamine base. At 5 a. m. she was given 50 mg. of hydrocortisone intravenously with no effect on her blood pressure or consciousness. Deslanoside (Cedilanid-D), 0.8 mg., and atropine, 1/150 grains (0.4 mg.), were given intravenously at 6:30 a. m. at the onset of a series of grand mal convulsions. At 8:30 a. m. one ampul of aqueous epinephrine, 1:1,000, was given intravenously with no improvement of her cardiovascular status. At 10 a. m. 50 mg. of hydrocortisone was given intravenously, but the patient was moribund and died at 10:40 a. m., 34 hours after the phentolamine test. The fetal heart tones were lost about eight hours prior to death. An immediate postmortem cesarean section was productive of a 1,350-Gm. (3-lb.), male, slightly macerated, stillborn fetus with petechial hemorrhages of the epicardium and pleura.

Autopsy revealed a pheochromocytoma of the left adrenal gland weighing 29 Gm., intrauterine pregnancy, bilateral bronchopneumonia, acute bilateral pyelonephritis, and passive hyperemia of the viscera. Sections of the tumor were sent to Mount Sinai Hospital, Cleveland, and the pathologist's report was that the sections exhibited the classic structure of the benign type of pheochromocytoma.

Comment

In pregnancy the presence of a pheochromocytoma can easily be missed, since hypertension during pregnancy is usually attributed to other causes. The hypertension in other reported cases has been attributed to preeclampsia, atypical toxemia, essential hypertension, renal disease, nervousness, and hysteria.[4] In most instances pheochromocytomas in pregnancy are initially misdiagnosed as toxemia of pregnancy.[5] Many of the clinical states that pheochromocytomas simulate have been summarized by Hutchison and co-workers.[6]

The signs and symptoms produced by pheochromocytomas in pregnant patients are not unique; they are essentially the same as those found in the nonpregnant person. Graham [2a] found headaches present in 55 of 100 unselected nonpregnant patients with pheochromocytoma; palpitations, the second most common symptom, were present in 38. Peelen and DeGroat [3c] stated that the most common complaint in their series was a disturbance of vision. The onset of symptoms may be aggravated by the pregnancy and become more prominent after gestation.[5] Because of several reported instances of sudden deaths in patients with pheochromocytoma, cases of sudden maternal collapse post partum should be investigated for this tumor, along with more common complications such as internal hemorrhage, embolism, and rupture of the uterus.

Investigations of patients suspected of having this tumor should include a complete history and physical examination; chest x-ray; electrocardiogram; urinalysis with culture, if indicated; blood urea nitrogen or nonprotein nitrogen determination; pyelogram; and phenolsulfonphthalein test, if indicated. Such specific tests as the pharmacological tests that have been developed in the last decade should be used judiciously. The most recent tests have been the determinations of plasma and urine levels of the pressor substances, which have been found to be significantly elevated during the active phase of a functioning tumor.[7] The levels of urinary pressor substances or catecholamines may be elevated due to anxiety.[6] In contrast to the pharmacological tests these plasma and urine analyses offer no risk to the patient.

One of the popular pharmacological diagnostic agents is phentolamine methanesulfonate, which was developed in 1947 and introduced in the early 1950's.[8] The actions of the hypotensive agents, such as phentolamine, depend on either chemical blocking of the ganglion or peripheral blocking action of the circulating pressor substances, or, possibly, both. The literature states that phentolamine can be used as a diagnostic agent in the office, as the effect of the drug is rapidly dissipated, which is one of the reasons for its popularity as a diagnostic and screening agent.[9] False-positive reactions to the phentolamine test commonly occur in patients who have received sedatives, cyanates, or narcotics or are uremic. All sedatives and hypotensive agents should be withheld for 48 hours before the administration of phentolamine. After the use of Rauwolfia derivatives the test should be withheld for at least four weeks, as these may be detected in the blood for as long as one month after discontinuance.[9] Phenobarbital has a similar effect.[10] In this case, because of the rapidly rising blood pressure and symptoms thereof, the test was performed 14 hours after cessation of all sedation and use of hypotensives, one of which was reserpine.[9a]

Green and Grimsley [8] reported two cases of vasomotor collapse after oral administration of 60 mg. of phentolamine. The blood pressure in these two patients, however, did not fall below 80/70 mm. Hg, and full recovery occurred in four hours after intravenous administration of dextrose and Trendelenburg positioning. In 1954 Ross [11] reported one case of prolonged hypotension, cardiac arrhythmia, and death after intravenous administration of 5 mg. of phentolamine in a 35-year-old nonpregnant woman who had apparently received no prior medication and was not uremic. No pheochromocytoma was found at autopsy; the cause of death was cerebral hemorrhage. Bierman and Partridge [12] reported the use of the benzodioxane (Benodaine) test in a 33-year-old nonpregnant woman who had received no prior sedatives. When 3 mg. of the total dose of 17 mg. was administered intravenously the patient promptly went into a shocklike state, and her pulse and blood pressure became imperceptible. The blood pressure rose within one minute to 270/140 mm. Hg without medication and returned to the base-line value gradually after one minute. The authors believed that the patient would have died if the full dose had been given. Emanuel and co-workers [9b] reported a case of prolonged hypotension, after a phentolamine test, which ended fatally in a 65-year-old woman who had been taking mephobarbital and procainamide hydrochloride for a cardiac arrhythmia. In spite of administration of procainamide, levarterenol, deslanoside, and phenylephrine intravenously her cardiac arrhythmia, vasomotor collapse, and subsequent coma did not respond and the patient died 30½ hours after the phentolamine test (our patient died 34 hours after the phentolamine test). A pheochromocytoma was found at autopsy in this patient. As in our case solutions of levarterenol temporarily maintained the blood pressure but later became ineffective, with the patient dying from central nervous system damage. This appears to suggest serious injury of the pressor-response mechanisms of the two patients. Perhaps the usual dosage of the adrenolytic agents is excessive for some patients with pheochromocytoma, as shown in the case reported by Bierman and Partridge with the use of benzodioxane.

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Dr. Richard C. Bates, Dr. Henry E. Malcolm, and Dr. Leo W. Walker aided in the management of the case and the preparation of this report. Dr. Harry Goldblatt reported on the pathological sections.

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MUCOLYTIC AEROSOL THERAPY FOR LIPID PNEUMONIA

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A patient was hospitalized for pneumonia in 1954 after working for a year as an insect exterminator. Polycythemia and severe clubbing of fingers and toes were present in addition to roentgenographic evidence of severe pulmonary damage. In 1956 he was found to have chronic pulmonary tuberculosis. Although the two conditions coexisted, they involved distinct areas in the lungs. The diagnosis of lipid pneumonia was verified in a biopsy specimen of lung tissue, and the condition cleared up on inhalation treatment with a mucolytic detergent aerosol. After antibiotic treatment the tuberculous process was also arrested, but the evidence of chronic hypoxia remained.

The various reactions to different oils such as animal or vegetable oil as well as liquid petroleum were studied experimentally by Pinkerton[1] in 1927 and 1928. He demonstrated that neutral vegetable oils produced little damage, with the exception of chaulmoogra oil which caused necrotizing pulmonary lesions, while some animal oils as well as mineral oil led to a more pronounced tissue reaction with proliferation of multinucleated giant cells and macrophages. The picture was similar to that in human pathology. With the attention thus focused on this condition, lipid pneumonia became widely recognized and many excellent accounts with detailed description of the clinical and pathological manifestations were recorded in the next 25 years.

In diagnosis, lipid pneumonia[2] may be easily confused with such conditions as carcinoma, sarcoidosis, tuberculosis, and fungus diseases. Diagnosis may be attempted by cytological studies of the sputum, needle aspiration of the lung, and lung biopsy. Roentgenographically, two main types of lipid pneumonia have been observed: a circumscribed involvement within the lobe, which can easily be mistaken for a tumor, and a diffuse type, more commonly encountered, which usually affects several lobes. In long-standing cases, fibrosis develops; calcification and hilar lymphadenopathy are rarely disclosed by roentgenographic studies.

In the type of lipid pneumonia[3] that is limited to a single lobe, lobectomy or segmental resection has been recommended. Until the use of mucolytic aerosol in the case herein reported, no treatment has been available for the diffuse type of lipid pneumonia.

A 31-year-old man had chronic pulmonary tuberculosis first diagnosed June 20, 1956. He was hospitalized at the Veterans Administration Hospital, Kerrville, Texas, from June 27 to Sept. 28, 1956, when he left against medical advice. He was again hospitalized at the Veterans Administration Hospital from Nov. 24, 1956, to March 6, 1957, when he again left against medical advice. He was given streptomycin, 1 Gm. daily, isoniazid, 300 mg. daily, and aminosalicylic acid (PAS), during his first hospital stay. During his second hospitalization he was given streptomycin, 1 Gm. two times weekly, and isoniazid, 300 mg. daily.

Four days after leaving the hospital for the second time, the patient had hemoptysis and was hospitalized at Brooke Army Hospital for a week. He was transferred to the Veterans Administration Hospital on March 20, 1957. On reviewing the records of the stay at Brooke Army Hospital, it was noted that he had previously been hospitalized there, in 1954, for treatment of what was called a primary atypical pneumonia involving the right upper lobe, right middle lobe, and left lower lobe. The patient dated clubbing of fingers and toes from the time that he had had pneumonia two years before admission to the Veterans Administration Hospital. He had started work as an insect exterminator about one year before developing the pneumonia and clubbing of fingers and toes in 1954. Some of his work included the use of oily sprays in closed spaces.

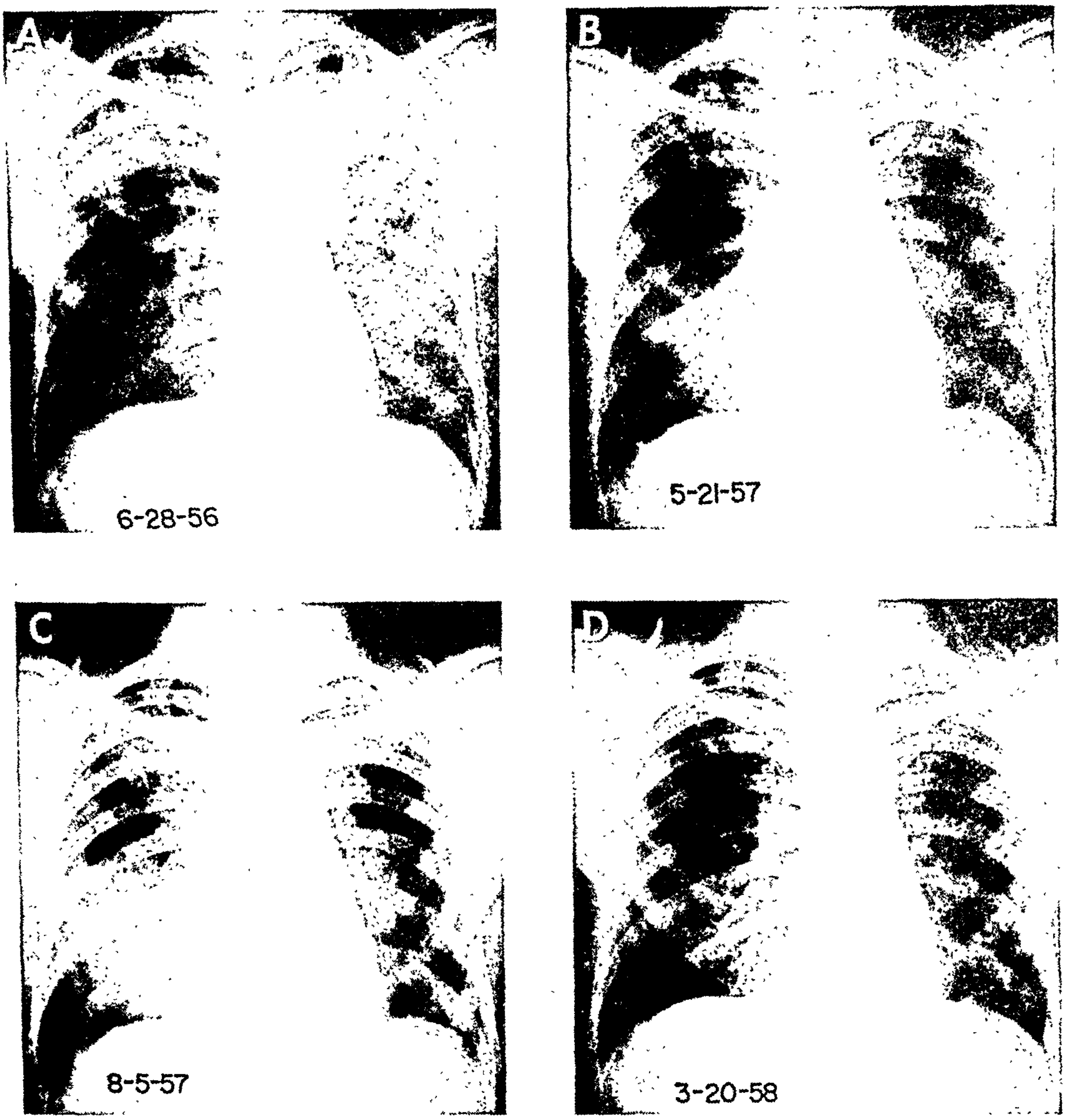
On admission of the patient to the Veterans Administration Hospital, June 27, 1956, severe clubbing of fingers and toes and many coarse inspiratory and expiratory rales throughout the left lung and in the middle and upper portions of the right lung were noted. He appeared to be quite ill, with a temperature of 103 F (39.4 C), severe cough, and moderate dyspnea. The admission roentgenogram (see figure, *A*) was described as showing severe, soft infiltration in the upper half of the lung, limited chiefly to the upper lobe, with evidence of cavitation. The left lung showed severe infiltration throughout, with probable cavitation in the apex.

The patient's hematocrit value was 49%; the sputum was consistently positive for tubercle bacilli on smear and culture. By January, 1957, the hematocrit value was 53%; by August, 1957, it was 59%, with a red blood cell count of 6,000,000 per cubic millimeter, and hemoglobin level of 118% (by the cyanmethemoglobin method; normal level, 15.6

From the Veterans Administration Hospital.

Gm. per 100 ml.). By October, 1957, the hematocrit value had risen to 64%, with a red blood cell count of 6,850,000 per cubic millimeter and hemoglobin level of 130%. Before the time of lung biopsy on Nov. 19, 1957, several venesections were done, and hematocrit values postoperatively stayed at 60% or below. Recent counts have shown consistent improvement, and a count taken Feb. 27, 1958, was similar to several others taken during January and February, 1958; the red blood cell count was 5,380,000 per cubic millimeter, hemoglobin level 118%, and hematocrit value 56%.

Scalene node biopsy showed lymphoid tissue and no evidence of malignant disease. A bronchial smear showed no malignant cells. Sputum cultures for fungi were negative, as were skin tests with coccidioidin, histoplasmin, and blastomycin. Results of a skin test to purified protein derivative 1 were positive. Collodion agglutination and complement-fixation tests gave negative results for histoplasmosis, blastomycosis, and coccidioidomycosis. Blood examination for lupus erythematosus cells gave negative results.



Roentgenogram showing, *A*, extensive bilateral pulmonary tuberculosis; *B*, development of pneumonitis, right base, after pulmonary tuberculosis had regressed to apices; *C*, more extensive involvement with pneumonitis on right and development of some pneumonitis of left side; and, *D*, clearing of pneumonitis due to lipid pneumonia.

On the present admission to the Veterans Administration Hospital, the patient again was given streptomycin, 1 Gm. two times weekly, and isoniazid, 300 mg. daily. It was felt that there had been regression of the tuberculous disease and that progress was satisfactory. However, fever, malaise, and dyspnea recurred, and a roentgenogram taken on May 21, 1957 (see figure, *B*) showed the development of a new lesion in the base of the right lung.

Broad-spectrum antibiotic therapy was started, and bronchoscopy was done. No evidence of endobronchial disease was found. The disease in the lower half of the right lung increased, and changes were seen in the lower half of the left lung.

Since Pseudomonas aeruginosa was isolated from the sputum several times, polymyxin B sulfate was given intramuscularly for two weeks. A roentgenogram taken on Aug. 8, 1957, (see figure, *C*) indicated an increase in disease in both lungs, and a diagnosis of pulmonary sarcoid along with tuberculosis was considered. Therapy with prednisolone, 25 mg. daily, was started. The right lung was diffusely involved, with complete involvement of the middle lobe, patchy diffuse involvement of the lower lobe, and a combination of tuberculosis and lipid pneumonia in the upper lobe.

When a lateral wedge of middle lobe was submitted for examination, the cut surfaces were fairly firm and displayed a lobulated, mottled, grayish brown-yellow pattern. Microscopic examination showed the alveolar septums to be thickened, the capillaries to be dilated, and the alveolar spaces to contain numerous foam cells and precipitated acidophilic material. Small accumulations of lymphocytes were seen throughout the sections. Special stain preparations were positive for fat.

The diagnosis was unresolved lipid pneumonia. Prednisolone therapy was continued during surgery and was discontinued only after the definitive diagnosis of lipid pneumonia was made. At a therapy conference, it was suggested that mucolytic aerosol therapy should be attempted. The agent in use at the Veterans Administration Hospital is Alevaire (a solution of 0.125% of a detergent called Superinone, 2% sodium bicarbonate, and 5% glycerine in water). Treatment was started Dec. 10, 1957. The patient was instructed in the use of a small hand nebulizer and inhaled about 10 cc. four times daily. There was an immediate increase in the production of thick sputum.

A roentgenogram taken March 20, 1958, (see figure, *D*) showed marked clearing of the lesions caused by the lipid pneumonia. The clubbing of fingers and toes had decreased about one-half. The patient's color had improved, and he was no longer dyspneic. He was obviously cyanotic and dyspneic until improvement in his condition became apparent; a study done Feb. 19, 1958, showed 70.5% of normal maximum breathing capacity, vital capacity 66% of normal, and ability to exhale 89.5% of his vital capacity in one second and 100% in two seconds.

Comment

The roentgenologist at the Veterans Administration Hospital noted the interesting fact that the extensive areas of tuberculous involvement delineated the areas of involvement with lipid pneumonia; the parts of the lungs involved with tuberculosis did not seem to become involved with lipid pneumonia when it appeared. It would seem that the pulmonary parenchyma had already been damaged by the presence of the oil but that alveolar filling had not yet taken place. This would be indicated by the marked clubbing and polycythemia. The history of exposure of two to three years before the final development of roentgenographically observable pneumonia is of interest. The fact that, although the lesions had cleared by x-ray therapy, the patient still had clubbing and moderate polycythemia would indicate that there had not been a complete cure.

Foe and Bigham[4] reported a case in which an oil spray caused a pneumonitis, which proved to be reversible. The oily mixture inhaled was 25% vegetable oil soap. The patient was hospitalized for three months with severe symptoms and was discharged on relief of symptoms but before any change was demonstrated in his roentgenogram, which had shown extensive diffuse pneumonia. Six months after discharge the patient was greatly improved and the multiple densities of both lungs had completely resolved. It would seem that the soapy mixture may have been a self-cleansing agent, just as in our case the detergent in the aerosol also seems to have acted as a cleansing agent.

In another case report[5] of acute lipid pneumonitis treated by steroid hormones, the patient fell, unconscious, into 5 in. of no. 5 crude oil; a great amount of this oil was aspirated into his right lung, and he suffered an acute pneumonitis. When broad-spectrum antibiotics were not helpful, it was felt that much of the patient's illness was due to the severe inflammatory reaction rather than to secondary bacterial invasion. After treatment with cortisone and ACTH the lipid pneumonia regressed completely, and after a year of therapy only a slight residual fibrosis remained.

In our case steroid therapy failed to cause improvement. The pulmonary tuberculosis in our patient continued to clear under therapy with antituberculosis drugs and prednisolone combined. However, the patient left our hospital against medical advice on May 6, 1958, and was readmitted on Aug. 13, 1958, for continued treatment of pulmonary tuberculosis. At time of readmission, and at present, there has been no evidence of recurrence of the lipid pneumonia. There is still moderate clubbing of the fingers, and the patient's hematocrit value has remained at 53% and his red blood cell count at 5,090,000 per cubic millimeter. During this most recent admission the pulmonary tuberculosis has showed evidence of healing in that the sputum has become negative for tubercle bacilli by smear and culture and planigrams of both lungs reveal no cavitation. Roentgenograms taken at the time of this writing show stable tuberculosis lesions and no recurrence of the shadows cast by the lipid pneumonia.

Summary and Conclusions

In lipid pneumonia the roentgenographically demonstrable symptoms may develop long after exposure to oily inhalations, although the symptoms of pulmonary insufficiency may be immediate. Residual alveolar damage is apparently still present in our patient, since clubbing and polycythemia persist, although to a lesser degree. Mucolytic aerosol therapy appears to be helpful in treating a patient with lipid pneumonia caused by the inhalations of oily solvents of an insecticide.

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TETANUS-LIKE REACTIONS TO PROCHLORPERAZINE (COMPAZINE)

REPORT OF EIGHT CASES EXHIBITING EXTRAPYRAMIDAL DISTURBANCES AFTER SMALL DOSES

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Patients reported developed extrapyramidal-type motility disturbances including masseter muscle spasm, loss of control and numbness of the tongue, tonic contractions of the sternocleidomastoid and trapezius muscles, oculogyric crises, back muscle spasms with opisthotonos, mask-like facies, and gross tremors. In some patients, symptoms could be mistaken as those of the primary disorder. Duration of reactions varied from 30 minutes to 48 hours. A disturbing fact is that small amounts that may be routinely prescribed are sufficient to produce these side-effects; thus, they are not the result of overdosage. Effective treatment is detailed in four case reports.

In many conditions in which nausea and vomiting are problems[1] prochlorperazine (Compazine), a phenothiazine derivative, is now being used and has been shown to be an effective antiemetic in a dose approximately one-half that of chlorpromazine (Thorazine) hydrochloride.

During the past few months, we have seen several patients who developed tetanus-like reactions after the administration of small doses of prochlorperazine. All but one had severe spasms of the jaw, and all remained mentally alert. With the trismus, all had one or more of the following extrapyramidal motility disturbances: (1) severe protrusion, loss of control, numbness, and athetoid movements of the tongue; (2) spasms of the sternocleidomastoid and trapezius muscles; (3) mask-like facies; (4) loss of associated movements in walking; (5) gross tremors and/or spasms of the upper extremities; (6) oculogyric crises; and (7) spasms of the back muscles, with opisthotonos.

Recent reports in the literature[2] alerted us to such disturbances due to prochlorperazine therapy and spared us much confusion when we were asked to see the patient in case 1. When this case was publicized in our 650-bed hospital, other physicians recalled similar experiences with patients receiving prochlorperazine. Due to this added awareness, almost one new incident per week is being found in our hospital.

A disturbing fact regarding the experience of our hospital so far is that the small amounts of prochlorperazine which are routinely prescribed are suffi-

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cient to produce these side-effects. In the majority of cases reported so far, larger doses of prochlorperazine have been incriminated.[3]

The purpose of this report is to further publicize this unusual reaction of certain persons to prochlorperazine therapy. The importance of this knowledge is obvious when a patient who may possibly develop tetanus has been receiving prochlorperazine while under observation. Christian and Paulson [2c] were aware of a similar danger when they stated that the drug may be used to control vomiting of central nervous system origin and that the reaction to the drug could be mistaken as a symptom of the primary disorder.

Four of the eight cases which we have observed will be discussed in detail; the essential features of all eight cases will be summarized in tables 5 and 6.

Report of Cases

Case 1.—A 27-year-old female was admitted on Dec. 6, 1958, with the chief complaints of crampy abdominal pain, nausea and vomiting, and abdominal enlargement of three days' duration. On examination, the only abnormal findings were those consistent with a diagnosis of partial mechanical intestinal obstruction. A "flat plate" roentgenogram of the abdomen suggested obstruction of the small intestine. This opinion was confirmed at operation on Dec. 18, 1958; a jejunal intussusception was found and corrected. In the preoperative period, this patient received prochlorperazine to control nausea. A list of all medicaments received prior to the reaction to the prochlorperazine is given in table 1.

Table 1.—*Medication Prior to Tetanus-like Reaction to Prochlorperazine of Patient in Case 1*

Day in Dec., 1958	Medication and Route	No. of Doses	Total Amount of Prochlorperazine, Mg.
6	Prochlorperazine 5 mg. q. 6 hr., I.M.	2	10
	Secobarbital (Seconal) 0.1 Gm., h s., oral	1	
7	Prochlorperazine 5 mg. q. 6 hr., I.M.	2	10
	Prochlorperazine 10 mg. q. 6 hr., I.M.	2	20
	Meperidine (Demerol) hydrochloride 50 mg., I.M.	5	
8	Prochlorperazine 10 mg. q. 6 hr., I.M.	2	20
	Promazine 25 mg. at 10:30 p.m., I.M.	1	
9	Prochlorperazine 10 mg. q. 6 hr., I.M.	2	20

At 6 p.m. on Dec. 8, 1958, the patient exhibited an unusual clinical picture, consisting of periodic spasms of her jaws and marked protrusion of her tongue, with an inability to speak. The entire episode persisted for approximately two hours. Promazine (Sparine) hydrochloride, 25 mg., was administered, intramuscularly, in an attempt to control these manifestations; the attempt was unsuccessful.

At 11 a.m. on Dec. 9, 1958, the periodic spasms of the jaw and protrusion of the tongue recurred. They were associated with grunting respirations, inability to speak or swallow, intermittent spasms of the sternocleidomastoid and trapezius muscles, and momentary periods of apnea. Neck rigidity was present, but could be overcome by passive manipulation. Between the paroxysms of spasm, which lasted from 5 to 20 minutes, an athetoid movement of the tongue and face was noted. The patient was conscious and alert during the entire period. The only additional abnormalities found on examination were an elevated blood pressure of 160/90 mm. Hg, sinus tachycardia (pulse rate of 128 per minute), increased deep tendon reflexes bilaterally, and an unsustained ankle clonus on the left side.

After blood had been obtained for electrolyte determinations, 5 ml. of a 10% calcium gluconate solution was given, intravenously, without appreciable effect. The results of the blood determinations were as follows: serum calcium level of 9.6 mg.%; serum sodium level of 141 mEq. per liter; serum potassium level of 3.2 mEq. per liter; and carbon dioxide–combining power of 58 vol.%. Amobarbital (Amytal) sodium, 0.25 Gm., was administered, intravenously; relief of the spasms was immediate and somnolence ensued. Administration of prochlorperazine was discontinued. Approximately six hours later there was a recurrence of the symptoms, which were again immediately relieved by the intravenous administration of 0.25 Gm. of amobarbital sodium.

For the following 24 hours, the patient had a mask-like facies and generalized slowing of all movements. None of the previously described disturbances recurred during the subsequent 20 days of hospitalization.

Case 2.—This patient had three tetanus-like episodes attributable to treatment with prochlorperazine. She was a 28-year-old female who was first admitted to our hospital on May 22, 1958, with the chief complaint of intermittent muscle spasms, on two occasions, during the preceding month. She was known to have a duodenal ulcer and had been receiving a convalescent ulcer diet, a liquid antacid (Maalox), 8 ml., orally, every four hours, and meprobamate (Milpath), one tablet, three times daily. One month prior to admission, because of an increase in her ulcer symptoms, one 25-mg. suppository of prochlorperazine had been administered. Twenty-four hours later, "uncontrollable muscular contractions of her neck and arms developed." All medication was promptly discontinued and the spasms subsided within six hours. One week later the meprobamate alone was administered, without incident.

During the week prior to admission, severe abdominal pain and vomiting developed. During the 24 hours preceding her admission to the hospital, she had inserted two 25-mg. suppositories of prochlorperazine, 12 hours apart. Eight hours after inserting the second suppository, severe recurrent spasms of the neck, causing flexion and rotation, developed. The tongue felt thick, the muscles of the back felt tight, both legs felt stiff, and the hands trembled; relief was attained by flexing the trunk. The patient's history and review of systems were noncontributory, except for a history of allergy to sulfonamides.

This patient was a well-developed, moderately dehydrated female, in obvious distress. There were intermittent spasms of the sternocleidomastoid and facial muscles, the face being pulled into a "fish-mouth" expression, with slight protrusion of the tongue. The blood pressure was 110/70 mm. Hg, and the heart rate 84 per minute. The only other abnormalities noted were symmetrical, hyperactive deep tendon reflexes and a bilaterally positive Hoffmann's sign. The diagnostic impressions of the examiner were tetanus, tetany, atypical epilepsy, idiosyncrasy to prochlorperazine, or conversion reaction.

The complete blood count and urinalysis were normal. No porphyrins were demonstrated in the urine. The serum calcium level was 9.8 mg.%, the inorganic phosphorus level 4.8 mg.%, and the alkaline phosphatase level 0.7 Bodansky units; results of the Kahn test were negative. Roentgenograms of the skull and hands were normal. Upper gastrointestinal tract studies demonstrated an active duodenal ulcer. Phenobarbital, 0.1 Gm., was given, intramuscularly, at the time of admission to the hospital, and the motility disturbances subsided in 8 to 10 hours.

The patient was readmitted to our hospital on Aug. 8, 1958, for the performance of a subtotal gastrectomy. This procedure was performed Aug. 15, 1958. The medicaments administered during the postoperative period are listed in table 2.

On. Aug. 18, 1958, two hours after administration of the last dose of prochlorperazine, the patient developed spasms of the jaw and protrusion of the tongue, but the trunk and extremities were not affected. The neurological examination was otherwise normal. Administration of prochlorperazine was discontinued, and 0.2 Gm. of sodium phenobarbital was given intravenously. All symptoms disappeared within one-half hour and did not recur. She was discharged from the hospital on Aug. 30, 1958, with a diagnosis of idiosyncrasy to prochlorperazine.

Table 2.—*Medication Prior to Tetanus-like Reaction to Prochlorperazine of Patient in Case 2*

Day in Aug., 1958	Medication and Route	No. of Doses	Total Amount of Prochlorperazine, Mg.
15	Meperidine hydrochloride 25 mg., I.M.	1	
	Promethazine (Phenergan) hydrochloride 50 mg., I.M.	1	
	Atropine sulfate 0.4 mg., I.M.	1	
16	Meperidine hydrochloride 75 mg., I.M.	3	
17	Meperidine hydrochloride 75 mg., I.M.	4	
	Prochlorperazine 10 mg., I.M.	3	30
18	Prochlorperazine 10 mg., I.M.	2	20

Case 3.—This 27-year-old female, gravida 5, para 2, who was two months pregnant, was admitted to our hospital on Oct. 31, 1958. Her chief complaints were nausea and vomiting of four weeks' duration and severe pain in the jaw and neck two hours before admission. She had been treated at home for nausea of pregnancy and had been taking 5-mg. tablets of prochlorperazine four times daily for the preceding four weeks. Twenty-four hours prior to admission, because of the onset of severe vomiting, she had received 10 mg. of prochlorperazine intramuscularly. Two hours before admission, during an episode of vomiting, she suddenly developed severe pain in her jaw and neck, her mouth was forced open, and she was unable to control her tongue, which protruded. Her physician noted these reactions, as well as marked spasm of the "strap muscles" of her neck. Meperidine hydrochloride, 100 mg., and sodium phenobarbital, 0.13 Gm., were administered intramuscularly. The symptoms disappeared within 30 minutes and did not recur.

Table 3.—*Medication Prior to Tetanus-like Reaction to Prochlorperazine of Patient in Case 3*

Day in Oct., 1958	Medication and Route	No. of Doses	Total Amount of Prochlorperazine, Mg.
29	Prochlorperazine 5 mg., oral	4	20
30	Prochlorperazine 5 mg., oral	4	20
	Prochlorperazine 10 mg , I.M.	1	10
31	Prochlorperazine 5 mg., oral	2	10

A history of occurrence of asthma during childhood and lifelong allergy to peanuts was obtained. At the time of admission to the hospital the physical examination was entirely normal.

There were no recurrences of the dystonic movements during four days of hospitalization, although she received prochlorperazine, 5 mg. intramuscularly once daily, during these four days. The medicaments given prior to the reaction on Oct. 31, 1958, are given in table 3.

Case 4.—This 64-year-old female was admitted to our hospital on Dec. 21, 1958, with the chief complaints of abdominal pain, diarrhea, nausea, and vomiting of two weeks' duration. The patient's history and review of systems were noncontributory. The blood pressure was 120/60 mm. Hg. The heart was enlarged 2 cm. to the left of the left midclavicular line, with a totally irregular rhythm and an average rate of 96 per minute. Tenderness was noted in the left lower quadrant of the abdomen. An annular stricture of the rectosigmoid region, probably carcinoma, was noted on barium enema examination. This was confirmed at the time of operation, on Jan. 1, 1959. An adequate resection of the mass was performed.

On Dec. 30, 1958, the patient developed a Parkinsonian and dystonic type of motility disturbance. During the preceding three days she had received the drugs indicated in table 4.

Six hours after the second dose of prochlorperazine she complained of tightness of the jaw and difficulty in speaking. Examination revealed athetoid movements and loss of control of the tongue, intermittent spasms of the masseter muscles, a mask-like facies, and a pill-rolling tremor of both hands. The remainder of the physical examination was essentially unchanged from the time of admission.

Administration of prochlorperazine was discontinued and phenobarbital, 0.1 Gm., was given orally. The attack persisted for eight hours. The patient was discharged from the hospital on Jan. 18, 1859, without any recurrence of these episodes.

TABLE 4.—*Medication Prior to Tetanus-like Reaction to Prochlorperazine of Patient in Case 4*

Day in Dec., 1958	Medication and Route	No. of Doses	Total Amount of Prochlorperazine, Mg.
27	Digitaline nativelle 0.1 mg., oral	1	
	Tetracycline (Cosa-Tetracyn) hydrochloride 250 mg. q. 4 hr., oral	6	
28	Digitaline nativelle 0.1 mg., oral	1	
	Tetracycline 250 mg. q. 4 hr., oral	6	
29	Digitaline nativelle 0.1 mg., oral	1	
	Tetracycline 250 mg. q. 4 hr., oral	6	
	Prochlorperazine 10 mg., I.M.	1	10
	Meralluride (Mercuhydrin) sodium 1 ml., I.M.	1	
	Succinylsulfathiazole (Sulfasuxidine) 1.0 Gm. q. 3 hr.	8	
30	Prochlorperazine 10 mg., I.M.	1	10
	Succinylsulfathiazole 1.0 Gm. q. 3 hr.	8	

Comment on Reactions.—In this group of patients, the symptoms most frequently seen were trismus and dyskinesia of the tongue (table 5). The smallest total dose of prochlorperazine associated with motor disturbances was 20 mg., given over a period of 24 hours (case 4). The disorder occurred irrespective of whether the oral, intramuscular, or rectal route of administration was used (table 6). In our small series of cases the ratio of females to males was 7:1. The patients ranged in age from 22 to 64 years. The duration of the motor disturbances varied from 30 minutes (case 3) to 48 hours (case 1).

Comment

Prochlorperazine is a relatively new antiemetic and tranquilizing agent, belonging to the large group of phenothiazine derivatives. Its chemical name is 2-chloro-10-[3-([illegible] pyl] phenothiazine. Oth[illegible]zine derivatives are chlorpromazine hydrochloride, promazine hydrochloride, triflupromazine (Vesprin) hydrochloride, promethazine hydrochloride, perphenazine (Trilafon), mepazine (Pacatal) acetate and hydrochloride, and thiopropazate (Dartal) dihydrochloride. Goldman [3a] states, "It is a noteworthy fact that all of these substances can produce Parkinsonism-like activity in practically any individual when the dosage level is high enough for a sufficient period of time." He found that the lowest dose of prochlorperazine which produced Parkinsonism was 30 mg. per day. In the case of perphenazine it was 12 mg. per day and with use of triflupromazine, 75 mg. per day.

TABLE 5.—*Incidence of Tetanus-like Symptoms After Administration of Prochlorperazine*

	Case No.								
Symptoms	1	2	3	4	5	6	7	8	Total
Trismus	+	+	+	+	+	+	+	+	8
Tongue disturbances	+	+	+	+	+	..	+	+	7
Tremors and spasms of extremities	+	+	+	..	..	+	..	+	5
Dysphasia and dysphagia	..	+	..	+	..	..	+	+	4
Torticollis	+	+	+	..	..	..	..	..	3
Mask-like facies	+	..	..	+	..	..	..	+	3
Opisthotonos	+	+	..	..	..	..	..	+	3
Oculogyric crises	..	..	..	..	..	..	..	+	1

There have been several reports of the development of Parkinsonism after administration of phenothiazine derivatives, one of the earliest being the report of Cohen.[4] Similar extrapyramidal reactions have been reported in the French [5] and German [6] literature. Hall and co-workers [7] found an incidence of 40% after the administration of chlorpromazine. Freyhan [2a] reported an incidence of 11.0% after administration of chlorpromazine and an incidence of 16.2% after administration of reserpine. Frierson [1b] reported an incidence of 33.3% after administration of prochlorperazine. The manufacturer [8] states that the incidence of reactions after administration of prochlorperazine is between 0.6% and 1.5%, if the daily dose is 40 mg., or below; 4.5%, if it is between 40 and 60 mg.; and 7.5%, if it is over 60 mg.

TABLE 6.—*Correlative Factors in Tetanus-like Reaction After Administration of Prochlorperazine (Compazine)*

Case No.	Amount of Prochlorperazine Given During 24 Hr. Preceding Reaction, Mg.	Route	Duration of Reaction Hr.	Other Phenothiazine Compounds Given
1	30	I.M.	48	Yes
2*	20	I.M.	12	Yes
3	30	Oral & I.M.	1	No
4	10	I.M.	8	No
5	40	I.M.	18	Yes
6	45	Oral	24	No
7	30	I.M.	25	Yes
8	20	I.M.	24	No

* Two reactions at home after use of prochlorperazine suppositories.

Freyhan [2a] feels that the term "neuroleptic drugs," introduced by Delay and others,[5] is far superior to the term "tranquilizers" when applied to this group of drugs. He states that the neuroleptic drugs produce reduction of psychomotor activity which results in diminished initiative and blunted emotional reactivation. The pharmacological action occurs at the subcortical level and involves various functional systems of the mesencephalon and the diencephalon. He states that the extrapyramidal syndrome is a regular effect of neuroleptic drugs, subject only to individual variations, reflecting the inhibitory action on psychomotor behavior. He points out that the significance of Parkinsonism must be seen in the fact that it demonstrates involvement of the striopallidal system, the system which regulates psychomotility. The therapeutic effects of the phenothiazine compounds must, therefore, be understood in terms of their influence on cerebral mechanisms which regulate psychomotility functions. One cannot, therefore, separate the therapeutic process from the action on the subcortical motor system.

The experience in our hospital with the production of extrapyramidal symptoms after the administration of small doses of prochlorperazine seems to substantiate Goldman's [3a] conclusion; namely, that these disturbances are not the result of overdosage but are a regular effect of such compounds on the subcortical motor system in certain susceptible persons.

With this conclusion in mind, it may be expected that the incidence of extrapyramidal manifestations after the administration of prochlorperazine will depend on the number of persons who are susceptible and the degree to which the drug is used. Six of the eight patients were seen in our 650-bed hospital in an eight-week period. This appears to be a high incidence when one considers the wide use of prochlorperazine over the past few years and the scarcity of reports of this type of disturbance when small doses are given. Part of the explanation of this seemingly high incidence may be that four of the eight patients were receiving other phenothiazine compounds concurrently with the prochlorperazine. It may well be that the combination of two or more phenothiazine derivatives will result in a higher incidence of dystonic aberrations than when either is used alone. It would be unwise, however, to draw any definite conclusions from the small series here reported.

As stated earlier, the intent of this report is to focus attention on the problem of the development of extrapyramidal motility disturbances after administration of prochlorperazine. This problem is important prophylactically, diagnostically, and therapeutically. The prevention of the development of this type of motor reaction is essential in situations in which such a reaction may mask the onset of tetanus, meningitis, encephalitis, or other neurological disturbances. This may be accomplished by withholding use of prochlorperazine, other phenothiazine derivatives, and reserpine in such situations. This problem has presented itself to others.[9] The recognition of this type of reaction is usually not difficult if it is suspected in any person who develops extrapyramidal motility disturbances while receiving prochlorperazine.

The therapy administered, with apparent success, to the patients discussed in this series consisted of the following measures: 1. Use of prochlorperazine and all phenothiazine derivatives was discontinued. 2. The patient was reassured. 3. For mild reactions, small doses of phenobarbital were given; for severe reactions, 0.25 Gm. of amobarbital sodium was given slowly intravenously, until the reaction subsided; in the case of prolonged reactions 0.25 Gm. of amobarbital sodium was given slowly intravenously, 0.13 Gm. of phenobarbital sodium intramuscularly, and 1 mg. of benztropine methanesulfonate orally, until the reaction subsided.

The use of amobarbital sodium and phenobarbital sodium in therapy is in agreement with the following statement of Christian and Paulson [2c]: "In view of the fact that the rigidity and tremor of Parkinson's Disease disappear with sleep, cautious induction of sleep may be the simplest effective treatment for such drug induced reactions." Early treatment is necessary if severe muscle spasms occur, to prevent complications such as dental injuries (case 4) and dislocations of the mandible.[2b]

It is hoped that this report will alert physicians to this type of reaction and serve to remind them that prochlorperazine is no exception to the rule applicable to all medicaments; namely, that the risks involved must be weighed carefully against the anticipated benefits. Prochlorperazine is a valuable addition to the pharmacopeia, as has been well attested by many reports.[1]

Summary

Eight patients, while receiving small daily doses of prochlorperazine (Compazine), developed extrapyramidal-type motility disturbances. These reactions consisted of spasms of the masseter muscles; protrusion, loss of control, numbness, and athetoid movements of the tongue; tonic contractions of the sternocleidomastoid and trapezius muscles; gross tremors; oculogyric crises; tonic spasms of the back muscles with opisthotonos; and a mask-like facies. The duration of these reactions varied from 30 minutes to 48 hours. No permanent after-effects developed.

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Administration of prochlorperazine was discontinued and phenobarbital, 0.1 Gm., was given orally. The attack persisted for eight hours. The patient was discharged from the hospital on Jan. 18, 1859, without any recurrence of these episodes.

TABLE 4.—*Medication Prior to Tetanus-like Reaction to Prochlorperazine of Patient in Case 4*

Day in Dec., 1958	Medication and Route	No. of Doses	Total Amount of Prochlorperazine, Mg.
27	Digitaline nativelle 0.1 mg., oral	1	
	Tetracycline (Cosa-Tetracyn) hydrochloride 250 mg. q. 4 hr., oral	6	
28	Digitaline nativelle 0.1 mg., oral	1	
	Tetracycline 250 mg. q. 4 hr., oral	6	
29	Digitaline nativelle 0.1 mg., oral	1	
	Tetracycline 250 mg. q. 4 hr., oral	6	
	Prochlorperazine 10 mg., I.M.	1	10
	Meralluride (Mercuhydrin) sodium 1 ml., I.M.	1	
	Succinylsulfathiazole (Sulfasuxidine) 1.0 Gm. q. 3 hr.	8	
30	Prochlorperazine 10 mg., I.M.	1	10
	Succinylsulfathiazole 1.0 Gm. q. 3 hr.	8	

Comment on Reactions.—In this group of patients, the symptoms most frequently seen were trismus and dyskinesia of the tongue (table 5). The smallest total dose of prochlorperazine associated with motor disturbances was 20 mg., given over a period of 24 hours (case 4). The disorder occurred irrespective of whether the oral, intramuscular, or rectal route of administration was used (table 6). In our small series of cases the ratio of females to males was 7:1. The patients ranged in age from 22 to 64 years. The duration of the motor disturbances varied from 30 minutes (case 3) to 48 hours (case 1).

Comment

Prochlorperazine is a relatively new antiemetic and tranquilizing agent, belonging to the large group of phenothiazine derivatives. Its chemical name is 2-chloro-10-[3-(1-methyl-4-piperazinyl)propyl] phenothiazine. Other well-known phenothiazine derivatives are chlorpromazine hydrochloride, promazine hydrochloride, triflupromazine (Vesprin) hydrochloride, promethazine hydrochloride, perphenazine (Trilafon), mepazine (Pacatal) acetate and hydrochloride, and thiopropazate (Dartal) dihydrochloride. Goldman [3a] states, "It is a noteworthy fact that all of these substances can produce Parkinsonism-like activity in practically any individual when the dosage level is high enough for a sufficient period of time." He found that the lowest dose of prochlorperazine which produced Parkinsonism was 30 mg. per day. In the case of perphenazine it was 12 mg. per day and with use of triflupromazine, 75 mg. per day.

TABLE 5.—*Incidence of Tetanus-like Symptoms After Administration of Prochlorperazine*

Symptoms	Case No. 1	2	3	4	5	6	7	8	Total
Trismus	+	+	+	+	+	+	+	+	8
Tongue disturbances	+	+	+	+	+	..	+	+	7
Tremors and spasms of extremities	+	+	+	..	..	+	..	+	5
Dysphasia and dysphagia	..	+	..	+	..	..	+	+	4
Torticollis	+	+	+	..	..	..	..	..	3
Mask-like facies	+	..	..	+	..	..	..	+	3
Opisthotonos	+	+	..	..	..	..	..	+	3
Oculogyric crises	..	..	..	..	..	..	..	+	1

There have been several reports of the development of Parkinsonism after administration of phenothiazine derivatives, one of the earliest being the report of Cohen.[4] Similar extrapyramidal reactions have been reported in the French [5] and German [6] literature. Hall and co-workers [7] found an incidence of 40% after the administration of chlorpromazine. Freyhan [2a] reported an incidence of 11.0% after administration of chlorpromazine and an incidence of 16.2% after administration of reserpine. Frierson [1b] reported an incidence of 33.3% after administration of prochlorperazine. The manufacturer [8] states that the incidence of reactions after administration of prochlorperazine is between 0.6% and 1.5%, if the daily dose is 40 mg., or below; 4.5%, if it is between 40 and 60 mg.; and 7.5%, if it is over 60 mg.

TABLE 6.—*Correlative Factors in Tetanus-like Reaction After Administration of Prochlorperazine (Compazine)*

Case No.	Amount of Prochlorperazine Given During 24 Hr. Preceding Reaction, Mg.	Route	Duration of Reaction Hr.	Other Phenothiazine Compounds Given
1	30	I.M.	48	Yes
2*	20	I.M.	12	Yes
3	30	Oral & I.M.	1	No
4	10	I.M.	8	No
5	40	I.M.	18	Yes
6	45	Oral	24	No
7	30	I.M.	25	Yes
8	20	I.M.	24	No

* Two reactions at home after use of prochlorperazine suppositories.

Freyhan [2a] feels that the term "neuroleptic drugs," introduced by Delay and others,[5] is far superior to the term "tranquilizers" when applied to this group of drugs. He states that the neuroleptic drugs produce reduction of psychomotor activity which results in diminished initiative and blunted emotional reactivation. The pharmacological action occurs at the subcortical level and involves various functional systems of the mesencephalon and the diencephalon. He states that the extrapyramidal syndrome is a regular effect of neuroleptic drugs, subject only to individual variations, reflecting the inhibitory action on psychomotor behavior. He points out that the significance of Parkinsonism must be seen in the fact that it demonstrates involvement of the striopallidal system, the system which regulates psychomotility. The therapeutic effects of the phenothiazine compounds must, therefore, be understood in terms of their influence on cerebral mechanisms which regulate psychomotility functions. One cannot, therefore, separate the therapeutic process from the action on the subcortical motor system.

The experience in our hospital with the production of extrapyramidal symptoms after the administration of small doses of prochlorperazine seems to substantiate Goldman's [3a] conclusion; namely, that these disturbances are not the result of overdosage but are a regular effect of such compounds on the subcortical motor system in certain susceptible persons.

With this conclusion in mind, it may be expected that the incidence of extrapyramidal manifestations after the administration of prochlorperazine will depend on the number of persons who are susceptible and the degree to which the drug is used. Six of the eight patients were seen in our 650-bed hospital in an eight-week period. This appears to be a high incidence when one considers the wide use of prochlorperazine over the past few years and the scarcity of reports of this type of disturbance when small doses are given. Part of the explanation of this seemingly high incidence may be that four of the eight patients were receiving other phenothiazine compounds concurrently with the prochlorperazine. It may well be that the combination of two or more phenothiazine derivatives will result in a higher incidence of dystonic aberrations than when either is used alone. It would be unwise, however, to draw any definite conclusions from the small series here reported.

As stated earlier, the intent of this report is to focus attention on the problem of the development of extrapyramidal motility disturbances after administration of prochlorperazine. This problem is important prophylactically, diagnostically, and therapeutically. The prevention of the development of this type of motor reaction is essential in situations in which such a reaction may mask the onset of tetanus, meningitis, encephalitis, or other neurological disturbances. This may be accomplished by withholding use of prochlorperazine, other phenothiazine derivatives, and reserpine in such situations. This problem has presented itself to others.[9] The recognition of this type of reaction is usually not difficult if it is suspected in any person who develops extrapyramidal motility disturbances while receiving prochlorperazine.

The therapy administered, with apparent success, to the patients discussed in this series consisted of the following measures: 1. Use of prochlorperazine and all phenothiazine derivatives was discontinued. 2. The patient was reassured. 3. For mild reactions, small doses of phenobarbital were given; for severe reactions, 0.25 Gm. of amobarbital sodium was given slowly intravenously, until the reaction subsided; in the case of prolonged reactions 0.25 Gm. of amobarbital sodium was given slowly intravenously, 0.13 Gm. of phenobarbital sodium intramuscularly, and 1 mg. of benztropine methanesulfonate orally, until the reaction subsided.

The use of amobarbital sodium and phenobarbital sodium in therapy is in agreement with the following statement of Christian and Paulson [2c]: "In view of the fact that the rigidity and tremor of Parkinson's Disease disappear with sleep, cautious induction of sleep may be the simplest effective treatment for such drug induced reactions." Early treatment is necessary if severe muscle spasms occur, to prevent complications such as dental injuries (case 4) and dislocations of the mandible.[2b]

It is hoped that this report will alert physicians to this type of reaction and serve to remind them that prochlorperazine is no exception to the rule applicable to all medicaments; namely, that the risks involved must be weighed carefully against the anticipated benefits. Prochlorperazine is a valuable addition to the pharmacopeia, as has been well attested by many reports.[1]

Summary

Eight patients, while receiving small daily doses of prochlorperazine (Compazine), developed extrapyramidal-type motility disturbances. These reactions consisted of spasms of the masseter muscles; protrusion, loss of control, numbness, and athetoid movements of the tongue; tonic contractions of the sternocleidomastoid and trapezius muscles; gross tremors; oculogyric crises; tonic spasms of the back muscles with opisthotonos; and a mask-like facies. The duration of these reactions varied from 30 minutes to 48 hours. No permanent after-effects developed.

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TEMPORAL ARTERITIS

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Temporal arteritis is a subacute or acute inflammation of the arteries occurring usually in people aged 55 or older. Inflammatory and degenerative changes in the vessel wall are histologically characteristic, but the cause is not known. Although the name does not imply it, arteritis is active in other vessels such as the aorta, ophthalmic, and internal carotid. Prior to induration and swelling of the temporal artery, there may be generalized manifestations such as chills, fever, sweats, weakness, anorexia, weight loss, and nonlocalized pain. The end-result of arteritis may be occlusion or rupture of the vessel, with secondary tissue changes due to lack of blood supply. Frequently, partial or total loss of vision which can be temporary or permanent results from ophthalmic arteritis. In the past, temporal arteritis has often gone unrecognized. It is worthy of diagnostic effort now because effective treatment is available. Corticosteroid therapy gives symptomatic relief and arrests progress of the disease.

Temporal arteritis is a disease of still unknown etiology. It was first described by Hutchinson in 1889.[1] Temporal arteritis was, however, first considered as a clinical and pathological entity by Horton and co-workers,[2] who described two cases in 1931. By 1946 30 cases had been described. Cooke and co-workers,[3] in an excellent review of the literature to date and a report of seven cases, contended that "there existed in elderly people a widespread arterial disease, not uncommon, but rarely recognized, in which characteristic arterial and striking local signs occurred and in which inflammatory and degenerative changes in the walls of the affected arteries produce a characteristic histologic picture." They contended that the syndrome they had observed was identical with that described by Horton and co-workers as temporal arteritis.

The arteritis was described by Horton and co-workers as follows: Peculiar circumscribed areas of what appeared to be granulation tissue were present in the adventitia of the blood vessels, which suggested granulomas. Infiltration of round cells was present in the adventitia around the vasa vasorum and to a slight extent in the media of the vessels. Hemorrhage was present in the media in some areas. The intima in many areas was markedly thickened; the basal portion appeared acellular, with superimposed cellular layers, which indicated that intimal proliferation had taken place in different stages. In some areas a small lumen was still present, whereas in others the lumen had been completely occluded by either cellular or acellular thrombi.

In 1951 Cardell and Hanley[4] reported the postmortem findings of one case and reviewed the autopsy reports of 12 of the 27 cases thus far reported. In these autopsy specimens the frequency of involvement of individual arteries was as follows: aorta, 11 times; internal carotid, 6 times; external and common carotid, subclavian, and iliac, 5 times each; temporal, coronary, innominate, and femoral, 3 times each; and hypogastric, radial, and pulmonary arteries, 1 time each. They felt that coronary involvement might be rare. However, 7 of the 27 patients had had ischemic heart disease. There was involvement of the ophthalmic arteries in two cases, with resulting optic atrophy and retinal changes observed clinically. In one case there was considerable internal carotid arteritis, with right-sided paralytic signs. Lesions of the aorta were common. One case was reported with partial rupture and limited dissection of the aorta. Gilmour, as quoted by Cardell and Hanley,[4] reported a rupture of an aneurysm involving the subclavian artery. Save for two ruptures the recorded complications were chiefly thrombotic. The lesions, they concluded, seem to be found chiefly in the smaller arteries, producing the picture of temporal arteritis, blindness due to involvement of the ophthalmic artery, or, less often, cardiac or cerebral ischemia.

Clinical Features

Temporal arteritis usually affects men and women about equally, past the age of 55 years. The average age of patients in one series was 67. One case, however, was reported in a young woman aged 22.[4] In Wagener and Hollenhorst's[5] series of 122 cases the youngest patient with ocular involvement was aged 60 and the oldest 83.

The onset of the disease may be slow and difficult, if not impossible, to recognize. It may be manifested by chills, fever, sweats, weakness, anorexia, weight loss, and pain in different parts of the body. Headache, not localized, may be a prominent symptom. The symptoms may vary widely according to the region affected. There may be symptoms of cerebral involvement, melancholia, disorientation, and occasional signs of more pronounced cerebral injury. In other cases the symptoms may be cardiac, gastrointestinal, or genitourinary in origin.

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Perhaps one week to six months later a local involvement may be manifest. If the temporal vessel becomes involved, the headache will then be localized there. The pain is often severe and throbbing. It resists ordinary analgesics and is apt to be worse at night. The involved artery becomes swollen, tender, hypersensitive, red, and nodular. Pulsation later ceases, and the vessel may become a firm, pulseless cord. Although temporal arteritis is an outstanding involvement Wagener and Hollenhorst found, in 66 patients with positive biopsy findings, only 32 who complained of tender large temporal vessels.

The importance of ocular involvement warrants special mention. This was emphasized by Wagener and Hollenhorst in 1956. They reported 122 cases in which 68 patients, or 56%, had ocular involvement. Of this number 54 had loss of vision; 15 had bilateral blindness and 18 had blindness in one eye. This complication may come on gradually; however, it is usually abrupt and not complete at first but progresses in a day or so. If one eye is affected, the second eye may become involved up to three weeks later. The longest interval between first-eye and second-eye involvement was two months. When blindness occurs, it is permanent. Sometimes the extraocular muscles become involved. This condition may vary from day to day and it usually clears.

Griffith[6] recently offered the concept of hypersensitivity as a background for accepting the belief that a common etiological factor underlies this disease, which he called nonsuppurative inflammatory arteritis. He said that the vascular lesions present in the collagen group of diseases were similar histologically and comparable to lesions found in the temporal arteritis described by Horton and coworkers.[2] He reported three cases of pulseless disease syndrome. A biopsy of the left subclavian artery in each patient showed inflammatory reaction of the adventitia and media. A third patient died, and at autopsy advanced arteriosclerosis was seen to be present.

Diagnosis.—The diagnosis of temporal arteritis may be suspected with a history of malaise, weakness, fever, anorexia, and weight loss in a patient past the age of 55. If involvement of a temporal or ophthalmic artery is present, and the sedimentation rate is elevated, the diagnosis is certain. Biopsy of an involved vessel will permit a definite diagnosis.

In the differential diagnosis one must consider brain tumor, secondary metastases, cerebrovascular accident, retinal artery thrombosis, sinusitis, neuralgia, neuritis, arthritis of the cervical spine, and dermatomyositis. A differential diagnosis between temporal arteritis, thromboangiitis obliterans, and periarteritis nodosum may be difficult.

The duration of the illness may be three to six months. One of the patients described by Cooke and co-workers[3] died after a 20-month illness.

Treatment.—Progress has been made in the treatment. It was recognized early that biopsy of the inflamed vessel gave relief of pain. Injection of procainamide along the involved artery also resulted in some relief from pain. Benefit was also reported from the intravenous administration of histamine and also from chlortetracycline. Cortisone was first used in the treatment of temporal arteritis in 1950.[7] This treatment has been most successful.

Birkhead and co-workers[8] in 1957 reported their results in a series of 55 patients treated with corticosteroids. These cases were proved by biopsy. Cortisone was given to most of them; the treatment was started as soon as the diagnosis was made. Three hundred milligrams of cortisone was injected the first day; then 200 mg. was injected daily, in divided doses every 12 hours. When improvement occurred and the sedimentation rate was near normal, the cortisone in doses of 200 mg. was given by mouth in divided doses every four hours for six weeks. Then the total dose was reduced. Three patients were treated with prednisone, 75 mg. and later 50 mg. daily, in divided doses every four to six hours for six weeks. One case was resistant, requiring 15 months of treatment. Anticoagulants and steroids were used in some who had had recent loss of vision. In this group there were no deaths. Twenty, or 36%, had some loss of vision. Five had bilateral blindness, and six had unilateral blindness. There was no improvement in the blind eyes, but no new bilateral blindness developed and none became blind with continued treatment. The authors believed that corticosteroids should be given in all cases as soon as possible. The steroids will control the arteritis as long as it endures and thus safeguard the degree of vision that remains, but whether the steroids promote histological healing is subject to question.

Report of Cases

Case 1.—A woman, aged 72, presented herself to one of us (E. H. B.) on Dec. 27, 1957, complaining of pain in the left side of the neck, extending to the left ear, of 10 days' duration. The pain moved into the left temporal area and into the left side of the jaw, so that chewing was difficult. After a few days pain came into the right temporal area. There was associated redness and swelling of the vessels. The pain was intermittent, throbbing in character, and worse at night. Application of heat and ingestion of aspirin gave some relief. She had no pain elsewhere, the history otherwise was negative, and her vision was good.

Physical examination revealed an asthenic elderly woman weighing 100 lb. (45.4 kg.). The temporal vessels were raised, tender, and inflamed, and nodules were felt along their course. Pulsation of these vessels was diminished. The external carotid vessels were also involved, to a lesser degree. The ocular fundi were grossly normal. The disks appeared normal, and no evidence of retinitis was present. The blood pressure was 170/110 mm. Hg. The aortic and pulmonary second sounds were regular and accentuated 2+. Brachial sclerosis, 2+, was present, but otherwise the results of examination were negative.

The laboratory examination showed the hemoglobin concentration to be 83%, the red blood cell count 4,250,000 and the white blood cell count

10,050 per cubic millimeter, with 75% polymorphonuclear cells and 14% lymphocytes. The sedimentation rate was 5 mm. in 15 minutes and 57 mm. in 45 minutes (Westergren). The blood urea nitrogen level was 9.5 mg.%. Results of serologic tests and urinalysis were negative. The serum cholesterol level was 292 mg.%. The electrocardiogram was abnormal, with changes compatible with myocardial ischemia. X-ray examination of the chest revealed calcification in the aortic knob. The heart was enlarged, and there were some changes in the left apex consistent with an old inflammatory process. The patient was admitted to the Emanuel Hospital for further diagnosis and treatment.

A biopsy specimen was taken from the left temporal artery. The specimen was firm and covered by a small amount of fibrous connective tissue. A microscopic section revealed the wall to be thickened, in part by arteriosclerosis (fig. 1). In a portion of the wall there was an inflammatory reaction with monocytes, plasma cells, and segmented neutrophil reaction, involving chiefly the adventitia and media, with a few cells extending into the region of the intima. The lumen of the artery was reduced in volume but appeared to be patent and free from thrombosis. The diagnosis was arteritis involving the temporal artery.

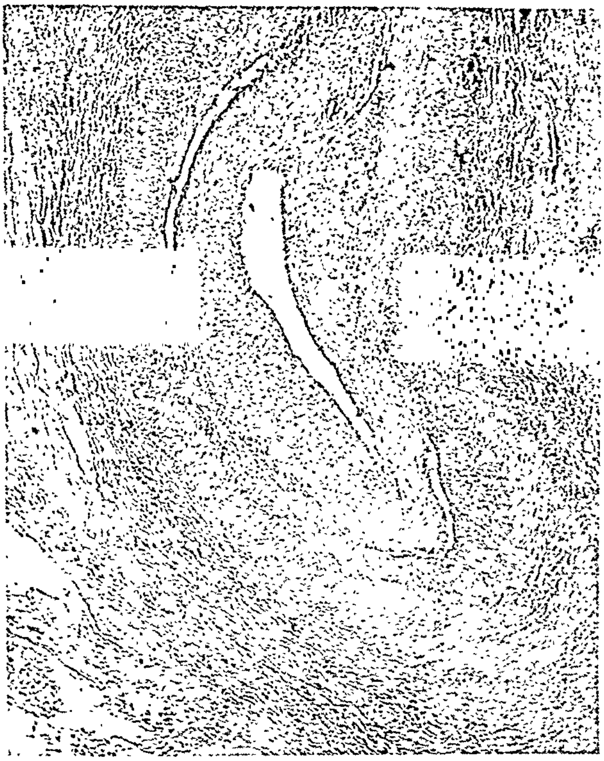

Fig. 1 (case 1).—Biopsy specimen from temporal artery. Note thickening of wall (× 30).

The patient was given 20 mg. of methylprednisolone (Medrol) daily in five divided doses. The next day she was free from pain for the first time. Two days later the signs of inflammation were diminishing. The blood pressure fell to 136/80 mm. Hg. Twelve days after the onset of treatment the vessels were not tender and appeared smaller. The patient then was discharged from the hospital on therapy with methylprednisolone, 14 mg. daily in four divided doses. She continued to be free of symptoms. The methylprednisolone dosage was gradually reduced and discontinued after a total of six weeks. The patient's progress has been followed for the past year and she has experienced no recurrence of her trouble.

Case 2.—A woman, aged 55, presented herself at the office of one of us (W. L. S.) on July 9, 1958, with a history of an influenza-like illness characterized by chills, general myalgia, headache, and a low-grade temperature elevation to 101 F (38.3 C) extending over the prior 10 days. Tender, firm, and ropy temporal arteries with scattered nodularity were palpable, which the patient said dated back to the onset of her clinical illness. General examination was not otherwise remarkable except for a blood pressure of 170/110 mm. Hg and general arteriolar constriction on funduscopic examination. Sedimentation rate was 29 mm. in 45 minutes (Westergren). A clinical diagnosis of temporal arteritis was made and symptomatic therapy only was instituted.

Over the next few days the patient felt subjectively improved and the temporal artery tenderness diminished. However, the vessels remained cord-like and firm, and a low-grade temperature elevation, 99 to 101 F (37.2 to 38.3 C), persisted. On July 14, 1958, she noted partial numbness and awkwardness of the right arm and leg on arising from bed and was hospitalized that morning for instigation of steroid therapy.

Physical examination on hospitalization revealed a gray-haired woman of good nutrition and stated age. Her temperature was recorded at 100 F (37.8 C). The temporal arteries were tortuous along the lateral forehead areas with a raised, cord-like consistency on both inspection and palpation, and the vessel pulsations were minimal. In addition numerous small nodularities were palpable as thickenings of these cord-like arteries, and moderate tenderness to touch was present. Blood pressure again was 170/110 mm. Hg and the fundus arterioles were generally attenuated, but no visual disturbance or field defect was present. Although the cranial nerve function seemed intact, definite weakness was present in the right arm and leg, and there was marked decrease of skilled movement in these right extremities. The reflexes themselves were not unusual, the Babinski signs were not present, and otherwise the physical examination was within normal limits.

Laboratory examination showed the hemoglobin concentration to be 12.4 Gm.%; white blood cell count was 8,600 per cubic millimeter, with 80% polymorphonuclear cells, 7% band forms, 10% lymphocytes, and 3% monocytes. The sedimentation rate was 5 mm. in 15 minutes and 39 mm. in 45 minutes. Result of urinalysis was negative except for a trace of albumin. Results of serologic tests were negative, and an electrocardiogram and a chest x-ray were both normal.

Prednisone therapy was begun immediately, in doses of 10 mg. taken orally every six hours. The temperature fell to normal the following day and remained normal thereafter. Temporal vessel tenderness also began decreasing on the day after admission, although the cord-like consistency was still present. On July 16, 1958 (second day after admission), biopsy of the left temporal artery was performed with the patient under local anesthesia. Examination of the microscopic sections confirmed the diagnosis of arteritis. Inflammatory cells were noted infiltrating the vessel wall and concentrated mainly in the adventitia (fig. 2). The cellular deposits were predominantly mononuclear, although some polymorphonuclear leukocytes as well as eosinophils were present.

On July 18, 1958, the patient's clinical response was excellent, and prednisone dosage was reduced to 5 mg. every six hours. The patient was discharged home on July 22, 1958, to continue the same dosage schedule. At this time she was completely relieved of any temporal artery tenderness, and objectively the vessel consistency had improved an estimated 85% toward normal. Steady improvement of a gradual nature in the strength of her right arm and leg also occurred during these nine days of hospitalization.

Follow-up examination on July 25, 1958, revealed the temporal arteries to be completely normal to palpation—soft and pliable with good pulsations. Sedimentation rate had fallen to 16 mm. in 45 minutes. On July 30, 1958, the patient continued to feel well and examination was normal, except for a minimal residual weakness in the right arm and leg and a blood pressure of 180/100 mm. Hg. Prednisone therapy was continued, but in slowly decreasing doses, and whole-root Rauwolfia was added to the medication.

Nineteen days later, while the patient was taking prednisone, 2.5 mg. three times daily, two small nodules appeared along the course of the right temporal artery. A slight increase in prednisone dosage was ordered, and slowly this vessel returned to normal. Prednisone dosage was again tapered and continued over the next several weeks.

On Oct. 12, 1958, administration of prednisone was stopped completely, and two days later the patient experienced a sudden short episode of complete inability to speak, without other neurological change. No changes in the temporal vessels were present, and the sedimentation rate was normal (15 mm. in 45 minutes). The serum cholesterol level was 241 mg.%. Again steroid therapy was employed but in low dosages, and the patient remained asymptomatic on numerous follow-up examinations thereafter. Administration of prednisone was discontinued for the final time on Dec. 17, 1958, as was the Rauwolfia, since the blood pressure had returned to 120/80 mm. Hg. She had received prednisone for a total of five months. No residue of the original hemiparesis was present subjectively or objectively, and the patient has remained well.

Comment

The etiology of this syndrome is unknown. Bacteriological studies have been unrewarding. The disease may be, as Griffith[6] suggests, a hypersensitivity response. It must be appreciated that this disease may affect arteries in different parts of the body. When hidden vessels are affected, the resulting febrile illness may be obscure, may be considered viral in nature, or may be mistaken for an arteriosclerotic degenerative disease. When superficial vessels, i. e., on the head, are inflamed and a biopsy is performed, a definite diagnosis may be established.

Previous experience and our own confirm the usefulness of corticosteroid therapy. It is important to institute therapy promptly, since progression of the disease is thereby arrested. This is important when ocular involvement exists. When recent thrombosis is present, anticoagulant therapy may be a useful adjunct. The duration of treatment may last six weeks or more.

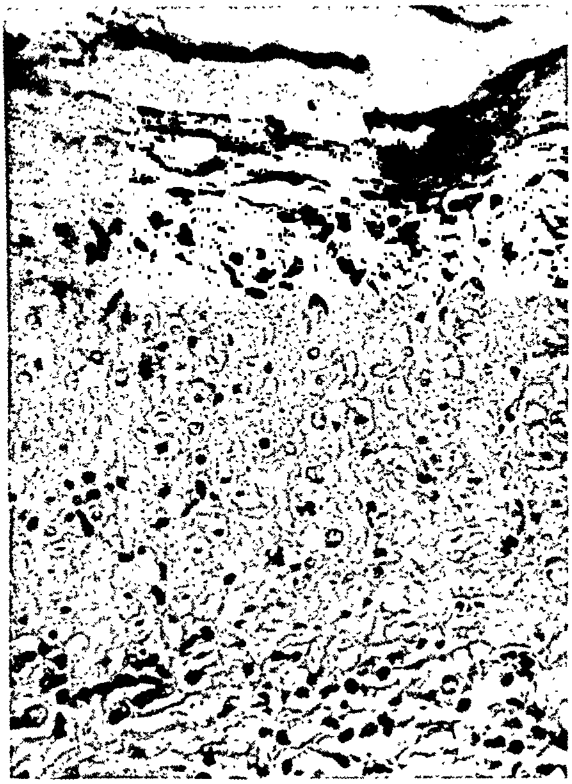

Fig. 2 (case 2).—High-power view of biopsy specimen, showing inflammatory reaction (× 400).

While temporal arteritis may affect more vessels than the name indicates, involvement of the temporal arteries still remains the constant and dominant feature of the disease.

Summary

Two patients with temporal arteritis were treated successfully. One had a vascular neurological complication. Both patients responded successfully to corticosteroid therapy, extending over periods of six weeks and five months respectively.

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PERCUTANEOUS TOPICAL ANALGESIA OF LARYNX AND TRACHEA

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It is possible to induce local anesthesia for certain diagnostic and surgical procedures by percutaneous topical analgesia of the larynx and trachea. This is done by an injection through the skin, subcutaneous fat, pretracheal fascia, and cricothyroid membrane (or cricotracheal ligament or soft tissues between the first and second tracheal rings). The anesthetic solution used was 2 to 3 cc. of 5% hexylcaine hydrochloride. The ensuing cough spreads the hexylcaine over the tracheolaryngeal mucous surfaces. The method has been used successfully in all but 54 of 10,204 cases. Failures were usually due to inexperience or poor technique. Severe coughing and occasional laryngospasm were the most frequent complications. The method is less cumbersome and time consuming than instillation of topical anesthesia via the mouth and rima glottidis, and it facilitates the passing of an endotracheal tube under difficult conditions.

Any new method in medicine should be accepted only after it has passed the test of time. Over a period of years this method should give, in the hands of various physicians, the same results with minimal complications. This study was undertaken to evaluate percutaneous topical analgesia of the larynx and trachea. Previous reports have described this method as translaryngeal analgesia,[1] transtracheal analgesia,[2] and transcricothyroid membrane anesthesia.[3] It is our belief that percutaneous topical analgesia of larynx and trachea is the correct and precise description of the method, since the topical anesthetic solution is instilled through the skin into the larynx or trachea and anesthetizes the mucous membrane of both structures.

We have collected the anesthesia records of 10,204 patients on whom percutaneous topical analgesia of the larynx and trachea was performed at the Memorial Center for Cancer and Allied Diseases over a four-and-one-half-year period and have reviewed them for results and complications.

Technique of Percutaneous Topical Analgesia of Larynx and Trachea

Topical anesthetic solution is instilled through the skin into the larynx or trachea. This is done by an injection through the cricothyroid membrane, or the cricotracheal ligament, or between the first and second tracheal rings which, in the midline, are covered by skin, sparse subcutaneous fat, and pretracheal fascia. The isthmus of the thyroid gland lies at or below the second tracheal ring and is usually not perforated. An injection at this level is almost painless and easily performed, although to the unaccustomed spectator it may look very unusual and even "barbaric." The cough produced by the anesthetic solution touching the mucous membrane spreads it over the tracheolaryngeal mucosa, vocal cords, aryepiglottic folds, and parts of the hypopharynx and glottis. This distribution has been observed after methylene blue dye was mixed with the anesthetic solution and injected in the usual way.

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In order to perform the injection the physician stands at the head of the supine patient, facing his feet. The thyroid, cricoid cartilages, and trachea are easily palpated after the head has been hyperextended. The larynx is kept steady with the index and middle fingers of one hand, leaving the midline free for the selected place of injection (see figure). The other hand, equipped with a 2-cc. or 5-cc. Luer-Lok syringe, introduces the attached 1.5-in., 20-gauge or 22-gauge needle through the aseptically prepared skin. After a short penetration a sensation is felt, similar to the penetration of the dura in a spinal tap, indicating that the needle lies in the lumen of the trachea or larynx. To insure the proper location of the needle, air is aspirated with the syringe, the anesthetic solution is then rapidly discharged, and the needle withdrawn. Slight pressure is applied over the site of injection to avoid a subcutaneous hematoma. The ensuing cough is usually mild, but may be of varying severity and duration. If this method of topical analgesia is indicated in patients who are awake, they are instructed not to swallow or cough until after the needle has been withdrawn.

We prefer to do this type of topical analgesia in patients who are asleep and will not remember the unusual injection in the neck. From 150 to 250 mg. of thiopental (Pentothal) sodium is given intravenously and the patient is ventilated with oxygen for several minutes. Then the injection is performed at the selected place. At times the cough that follows may be quite distressing and an additional injection of 50 to 100 mg. of thiopental sodium will alleviate it or, if the anesthesiologist becomes alarmed, 40 mg. of succinylcholine chloride will terminate it rapidly. For endoscopic work the mouth and pharynx are also sprayed with the topical anesthetic solution.

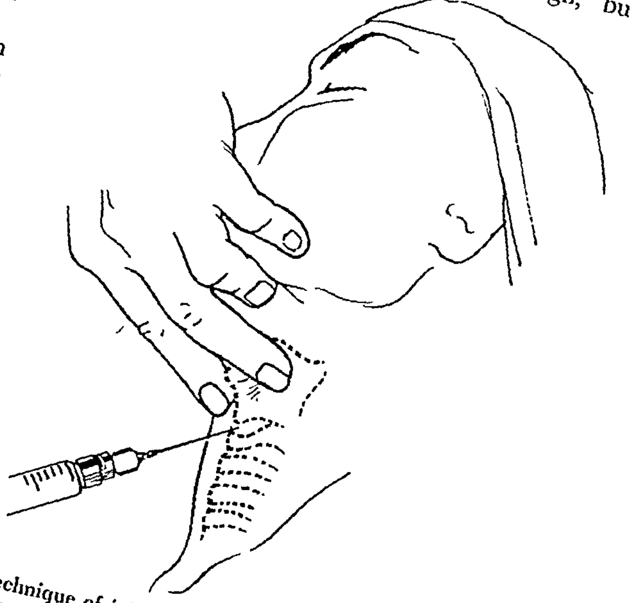
We have used 2 to 3 cc. of 5% hexylcaine (Cyclaine) hydrochloride solution for the percutaneous injection, because it acts rapidly and the analgesia is adequate. A 10% solution of cocaine produces excellent analgesia of the mucous membrane of the larynx and trachea, but the fact that it cannot be kept on the anesthesia machine for ready availability makes its use impractical. Other topical anesthetic solutions can also be used.

Indications for Percutaneous Topical Analgesia of Larynx and Trachea

The numerous uses of this type of topical analgesia will be considered according to relevant indications.

Routine Endotracheal Intubation.—A good topical analgesia of the larynx and trachea in a sleeping patient permits an unhurried endotracheal intubation, because ventilation has not been depressed by the administration of muscle relaxants. This is very important in the so-called anatomically difficult intubations. The anesthesiologist knows that the time available to pass the endotracheal tube is not limited, and he avoids brisk manipulations and force which may lead to undesirable sequelae. The amount of thiopental sodium administered should be sufficient to make the laryngoscopy easy without unduly depressing the respiration. One should not hesitate to use succinylcholine chloride in cases where extreme muscle relaxation is required. However, with sufficient experience that is seldom the case. This type of intubation is an invaluable teaching method for the young resident in anesthesiology.

Light Anesthesia.—The recent trend in anesthesiology is to maintain as light a plane of anesthesia as possible, avoiding the administration of large amounts of anesthetic agents followed by undesirable effects on the cardiovascular, respiratory, and other body systems. This is especially applicable to the poor-risk patient. Often the anesthesiologist has to introduce an oral airway or endotracheal tube in anesthetic planes in which the patient is analgesic but would not tolerate manipulations in the air passages and will cough, "buck," or have a laryngospasm. All of this can be eliminated by having the mucosa of the larynx and trachea anesthetized while maintaining the desirable plane of light anesthesia.



Technique of injection for percutaneous topical anesthesia of larynx and trachea.

Endoscopic Procedures.—Direct laryngoscopy, bronchoscopy and esophagoscopy are easily performed in a sleeping and adequately ventilated patient under percutaneous topical analgesia of the larynx and trachea. Additional topical analgesia of the mouth and pharynx is essential for smooth anesthesia in these instances.

Endotracheal Intubation for Intestinal Obstruction.—In the patient with intestinal obstruction, the skill of the anesthesiologist often determines the smoothness of the postoperative course. The ever-present danger of vomiting and aspiration during the induction of anesthesia should be eliminated by endotracheal intubation with a cuffed tube while the patient is awake and in control of his reflexes. A percutaneous topical analgesia of the larynx will anesthetize the mucosa but will not prevent the aryepiglottic folds from closing if vomiting occurs. Gentle laryngoscopy is necessary to make the patient cooperative and, with patience and perseverance, intubation can be accomplished.

Laryngospasm.—A well-developed laryngospasm can be broken with percutaneous topical analgesia of the larynx. But in such tense moments this method should be used only if a topical anesthetic solution and a syringe with attached needle are readily available. Time should not be wasted looking for them while a muscle relaxant can be given intravenously or sublingually.

Tumors of Larynx and Pharynx.—Tumors of the larynx and pharynx often reduce or distort the normal air passages, thus making intubation a very difficult procedure. These patients should be intubated while awake and in control of their respiratory, glossopharyngeal, and laryngeal muscles which will keep open the remaining airway until the endotracheal tube has been passed. An injection into the larynx or trachea and a spray with a topical anesthetic solution will provide the desired analgesia of the mucous membranes. Again a gentle handling of the laryngoscope is necessary to avoid bleeding from the tumor. In spite of all these precautions the surgical team should be ready to perform a tracheostomy if the need for one should arise.

Contraindications for Percutaneous Topical Analgesia of Larynx and Trachea

In the following instances percutaneous topical analgesia is impossible or less advisable: 1. Infection at the possible site of injection. The contraindication in this instance is too obvious to require any comment. 2. Very large tumors in the neck region obscuring the pertinent landmarks. This is a relative contraindication and depends on the experience of the operator. 3. X-ray radiation to the lungs or an asthmatic syndrome may render the trachea hypersensitive, so that an endotracheal tube passed quickly when the patient is under topical analgesia of the larynx and trachea and has been given an intravenous injection of thiopental sodium may produce a brochospasm. This again is a relative contraindication, depending on the possibility of maintaining during the operation an unobstructed airway at all times. 4. Patients having poor cardiac reserve or suffering from cardiac failure should not be subjected to the possibility of a prolonged cough. Hence, topical analgesia of larynx and trachea should be undertaken with care.

Complications

The possible complications of percutaneous topical analgesia of larynx and trachea fall into the following two groups.

Toxic Reaction due to the Topical Anesthetic Agent.—Toxic reaction due to the topical anesthetic agent is a possibility but, with amounts of up to 250 mg. of hexylcaine chloride or 200 mg. of cocaine, we have not observed any untoward symptoms from the cardiovascular or central nervous systems. The administration of ultra-short-acting barbiturates prior to the topical analgesia may have been a factor in preventing the development of toxic reactions.

Complications due to Technique.—A small subcutaneous hematoma at the site of injection has been observed and its prevention described. Some patients have a small vein running in the midline in front of the larynx and trachea. Damage to this vein during the injection should be scrupulously avoided.

The cough which follows the instillation of a topical anesthetic agent into the larynx or trachea could be severe and prolonged at times. As explained before, an additional administration of thiopental sodium, or succinylcholine chloride in severe cases, will abolish it rapidly.

In some patients slight bleeding in the trachea has been observed during laryngoscopy. This bleeding is self-limiting and of no consequence.

The possibility of breaking the needle during injection, creating a fistula, or an infection at the site of injection is ever present but has not been observed by us.

Results

Ten thousand two hundred four percutaneous analgesias of the larynx and trachea have been performed at the Memorial Center for Cancer and Allied Diseases in the past four and one-half years on patients who were anesthetized for various surgical procedures. One out of every three patients undergoing an operation received this type of topical analgesia. Fifty-four attempts to anesthetize the larynx and trachea percutaneously were classified as unsuccessful, the main reasons being inexperience or a plugged needle. One hundred thirty-six patients had a severe cough, and in 56 various degrees of laryngospasm were recorded. In 6 patients there was a subcutaneous hematoma at the site of injection, and 10 had a small amount of bleeding in the trachea. The topical analgesia of the laryngotracheal mucosa was produced in 414 patients by the administration of 200 mg. of cocaine (10% solution), while 100 to 250 mg. of hexylcaine chloride (5% solution) was administered to the remaining patients in this series.

Comment

Percutaneous topical analgesia of the larynx and trachea has been used with gratifying results by all members of the anesthesia staff at the Memorial Center. It is especially convenient for the residents, who are thus enabled to learn laryngoscopy without exposing the patients to hypoventilation.

This type of topical analgesia was started as a translaryngeal block through the cricothyroid membrane, but soon it was realized that the injection was made many times through the cricotracheal ligament or between the first and second tracheal rings. All of these three points of injection are very close together and actually it does not matter where the anesthetic solution is injected, because the ensuing cough will spread it over the mucous membrane of the trachea and larynx. It may be said that the topical anesthetic solution might be instilled into the larynx and trachea with a cannula via the mouth and rima glottidis. This is true, but after using this approach for over a year we found it to be cumbersome and time consuming. A single injection, preferably of a 5% hexylcaine (Cyclaine) solution, through the skin will provide the desired topical analgesia without any instrumentation; the laryngoscope needs to be inserted only once and that for the actual intubation.

This technique has provided us with the best conditions for passing an endotracheal tube under the most difficult circumstances. These are extensive tumors in the neck; anatomic distortions after radical surgery in the head and neck region; a full stomach; in laryngoscopy and bronchoscopy; and for production of a smooth, light anesthesia without bucking or coughing on the endotracheal tube.

The incidence of complications is minimal. Most of them can be avoided by strict adherence to the technique described. This method is easy to perform and can be mastered in a short period of time. It is our conviction that, if a new technique in anesthesia is still in use after the initial period of enthusiasm has faded, then this method has proved itself to be of value and should be applied more often. After performance of 10,204 percutaneous topical analgesias of the larynx and trachea we believe that this method is reliable and safe, with minimal complications.

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CLINICAL NOTES

KARTAGENER'S SYNDROME WITH LYMPHOSARCOMA OF SMALL INTESTINE

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Reports of unusual cases are justified by the fact that each account further adds to the accumulated knowledge of a particular problem. With this in mind, a case of Kartagener's syndrome with lymphosarcoma of the small intestine is reported.

Kartagener's syndrome, sometimes referred to as K's triad, consists of situs inversus viscerum, bronchiectasis, and paranasal sinusitis. Reports in the literature of some cases of this syndrome, however, have represented the third member of the triad as agenesis of the frontal sinuses.[1] In 1887 Fisher described total situs inversus, and in 1904 Siewert[2] reported the first case of situs inversus with bronchiectasis in a 21-year-old male. In Vienna, Kartagener[3] had, by 1935, collected 11 cases and added sinusitis to the organ transposition and pulmonary features, thus establishing the triad which bears his name today. Two years later, in 1937, Adams and Churchill[4] published the first report of two cases in the English language. Olsen[5] reported 14 cases, and Torgersen,[6] in 1947, described 28 cases in a survey. Eighty-two cases had been reported by 1950 in a collected case tabulation by Bergstrom and associates.[7] A total of 104 cases of Kartagener's syndrome had been described in the literature by 1955.[8] Clear-cut roentgenographic evidence of bronchiectasis had been presented in only 16 of the first 80 cases,[7] however, bronchography demonstrated bronchiectasis in the succeeding 30. The oldest patient reported at the time of writing was 63 years old[9] and the youngest 5 years of age.[10] Of the 110 patients heretofore described in the literature, the present patient is the oldest to be reported and the first with Kartagener's syndrome in association with lymphosarcoma.

Report of a Case

A 69-year-old World War I veteran was admitted to St. Elizabeth Hospital with a 10-day history of intermittent, cramping, periumbilical, and right-sided pain, anorexia, nausea, and vomiting. His abdomen had become progressively distended but he was passing flatus rectally. The patient believed that he had lost 10 lb. (4.5 kg.) of body weight in the past few months. There was a history of several instances of "flu" and pneumonia and a period of hospitalization in 1928 for pulmonary tuberculosis. He had a chronic cough, pro-

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From the Department of Surgery, St. Elizabeth Hospital.

ductive of yellow-green "phlegm" as well as a chronic postnasal discharge. No members of his family were known to have any congenital anomalies and there was no relevant family history. This man had smoked a pipe regularly for 40 years.

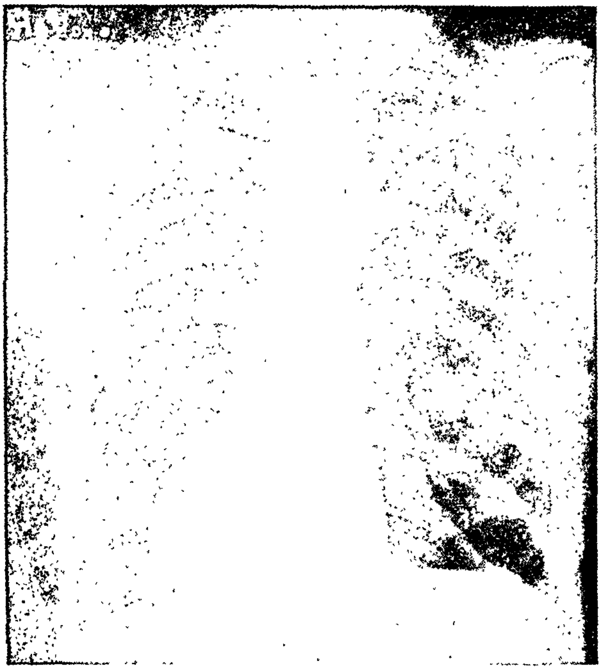

Fig. 1.—Roentgenogram of chest showing dextrocardia.

Physical examination revealed a man appearing acutely ill. The abdomen was distended and there was generalized abdominal tenderness, more prominent in the periumbilical region. Intestinal sounds were hyperactive but there were no masses or rigidity. A mucopurulent postnasal discharge was present, with a moderately injected pharynx. The chest was symmetrical but there was an increase in the anteroposterior diameter. Inspiratory and expiratory wheezes were present over both lung fields, and coarse rhonchi were heard. There was no dulness to percussion. The right heart border was found to be in the right midaxillary line, 7 cm. lateral to the right sternal border. A grade 1 systolic murmur was heard over the base of the heart and the heart sounds were diminished over the left side of the thorax. The blood pressure was 180/90 mm. Hg, with a regular heart rate of 88 per minute. The prostate was enlarged to grade 2 and was symmetrical, without nodularities or palpable irregularities in the rectal mucosa. The extremities showed signs of clubbing of the fingers but no cyanosis. Results of neurological examination were negative. Palpable, nontender, enlarged cervical and axillary lymph nodes were noted.

On admission the white blood cell count was 10,450 per cubic millimeter, with 81% neutrophils, 10% lymphocytes, 3% monocytes, and 4% eosinophils. The hemoglobin level was 13.3 Gm.%, with a hematocrit value of 43%. Results of serologic examination and urinalysis were negative, and the level of nonprotein nitrogen was 28 mg.%. A chest x-ray revealed dextrocardia with a moderate amount of left ventricular enlargement (fig. 1). A flat plate of the abdomen demonstrated situs inversus with a considerable amount of gas in the intestinal tract, mainly in the colon. Barium and fluoroscopic studies confirmed the presence of situs inversus (fig. 2) and suggested a filling defect in the cecum, but could not be evaluated accurately because of ptosis of the large intestine and an overlying, distended small intestine. A small polyp was removed through the sigmoidoscope at the 15-cm. level and reported by the pathologist to be a mucosal rectal polyp with marked lymphoid infiltration.

Ten days after admission the patient's abdomen was still somewhat distended and he continued to have intermittent abdominal cramps but no vomiting. He was taken to the operating room with a preoperative diagnosis of partial intestinal obstruction. At surgery he was found to have, in addition to complete transposition of the abdominal viscera, markedly enlarged mesenteric lymph nodes. Numerous areas of thickened, annular, pale-colored segments, with raised, firm serosal edges, were seen in the jejunum and ileum. Throughout the small intestine were small, firm, palpable nodular tumors within the intestinal lumen. The entire wall of the cecum was markedly thickened and pale in color. Proximal to the ileocecal valve the ileum was distended, and there was a marked narrowing of the ileocecal valve. Five inches of the terminal ileum and all of the cecum were resected, with restoration of gastrointestinal continuity by an end-to-end anastomosis. In addition, an excisional biopsy specimen was taken of one of the enlarged mesenteric lymph nodes. The finding of the pathological

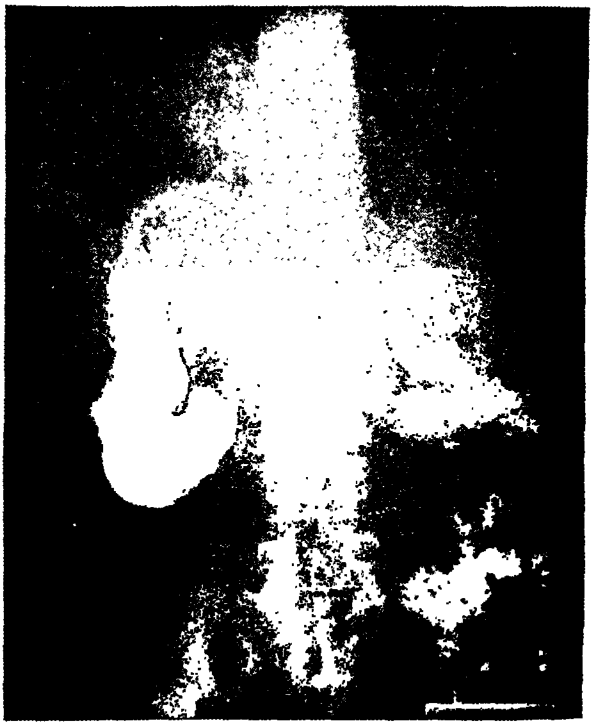

Fig. 2.—"Barium swallow" of stomach showing transposition of abdominal viscera.

reports on the resected specimen and the lymph node was lymphosarcoma (fig. 3). The patient convalesced uneventfully until the 10th postoperative day, when his abdomen again became distended and he began to vomit. A Miller-Abbott tube was used for intestinal decompression, which satisfactorily relieved him, and one week later it was removed. The patient received a course of nitrogen mustard therapy intravenously (0.2 mg. per kilogram of body weight) over a three-day period. Roentgenograms were then taken of the paranasal sinuses which showed some opacity in the left maxillary antrum (fig. 4). A bronchogram revealed definite evidence of bronchiectasis in the posterior and lateral basal segments of the right lung (fig. 5). These examinations were carried out to confirm the diagnosis of Kartagener's syndrome. The patient was dismissed one month after his admission and is now receiving, as an outpatient, deep x-ray therapy to the abdomen for the lymphosarcoma.

Comment

Most physicians can recall having seen but one or two cases of situs inversus in a lifetime, since this congenital anomaly occurs only in about 1 in 8,000 persons.[6] Bronchiectasis is found in from 12 to 23% of persons with situs inversus but in only 0.3 to 0.5% of the general hospital and clinic population.[11] Hence it can be postulated that Kartagener's syndrome could occur in about 1 in 50,000 persons.

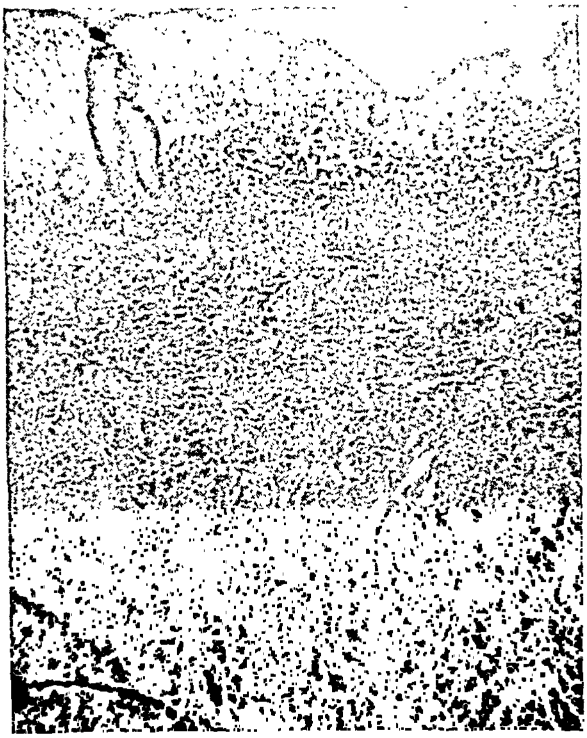

Fig. 3.—Photomicrograph of resected specimen of small intestine showing marked infiltration with lymphosarcoma.

Strictly speaking, the third member of the triad need not be present, for sinusitis occurs in approximately 90% of the cases of bronchiectasis. These two conditions therefore have a causal relationship, the former having been accepted as a factor in the etiology of the latter.[10]

The coincidence of bronchiectasis and situs inversus, which demonstrates that bronchiectasis occurs in 12 to 23% of cases of transposition of the viscera, supports the hypothesis advanced by Kartagener and others that hereditary predisposition probably is an important factor in certain cases of bronchiectasis. Sauerbruch [12] contended that 80% of cases of bronchiectasis are congenital. Olsen [5] at the Mayo Clinic felt that bronchiectasis is primarily due to some congenital anomaly of the bronchial walls which makes them more vulnerable to the factors of bronchial obstruction and infection. He presented 85 cases of true congenital dextrocardia. Of these 85 cases, 16.5% of the patients showed evidence of bronchiectasis, and half of these patients had had symptoms as far back as they could remember. The frequency of bronchiectasis generally is about 30 times as great among persons with situs inversus as among a representative clinical population. Dextrocardia and transposition of the great vessels may mechanically interfere with the flow of bronchial secretions and thus aid in the production of bronchiectasis, according to Karani.[13] Richards [10] expresses doubt that even gross infection can of itself, without a contributing cause, produce bronchiectasis. For instance, one may see many cases of purulent bronchitis with copious sputum and physical findings suggestive of bronchiectasis, and yet these patients may still have a normal

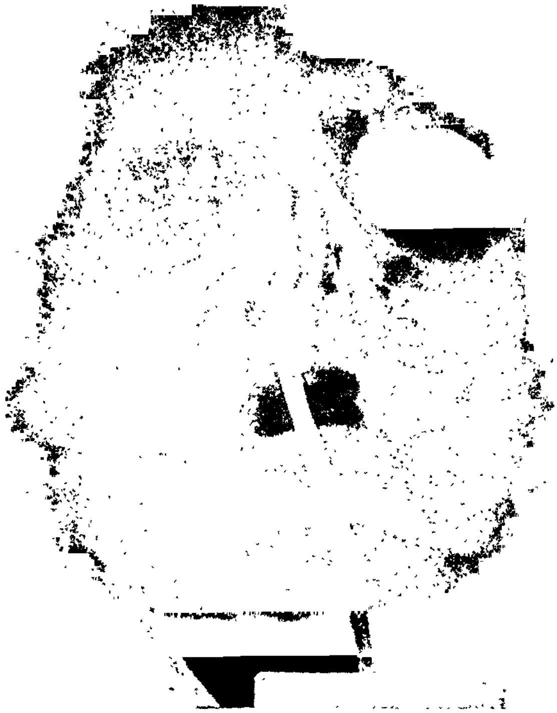

Fig. 4.—Roentgenogram of sinuses showing marked opacity of left maxillary antrum. Miller-Abbott tube in place for intestinal decompression. Incidental foreign body in right eye acquired in childhood accident.

bronchogram. Churchill,[14] in 1949, proposed that bronchiectasis in the Kartagener triad is a secondary manifestation and that the basic abnormality may be an altered secretory activity of the respiratory mucosa. It is apparent that, while some interesting concepts have been formulated, no definite final statement can be made as to the pathogenesis of bronchiectasis in Kartagener's syndrome.

Congenital transposition of the viscera is described by teratologists as the result of arrested development at some stage of embryonic growth. Exactly what disturbing influence precipitates the arrest is not definitely known. Cockayne[15] found that, when monozygotic twins were born into affected families, either both or neither had transposition of the viscera. No known member of the family of the patient here reported had had any congenital defects. Adams and Churchill[4] suggested that two types of people are affected by transposition of the viscera. "Mutants" have situs inversus but no other known congenital anomalies, while "monsters," aside from having situs inversus, have also associated congenital defects. Since the patient presented here showed no evidence of any other abnormality he is of the "mutant" variety.

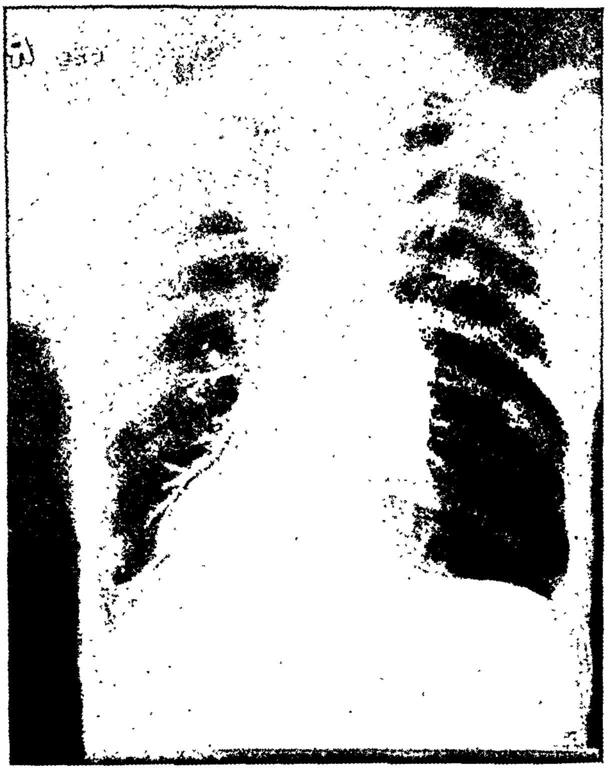

Fig. 5.—Bronchogram of right lung showing bronchiectasis in posterior and lateral basal segments.

The etiology of lymphosarcoma seems to be obscure, but it is classed as a malignant neoplasm. In this presentation its occurrence together with situs inversus has no probable relationship to its etiology; it is of interest because of its rarity.

Awareness of this interesting syndrome is necessary to the practicing physician, because the patient can be offered definite therapy for bronchiectasis which will greatly reduce his symptoms and later complications. It is therefore no longer sufficient to inform the patient of transposition of the abdominal viscera to prevent any error in diagnosis from contralateral abdominal signs. The patient should be investigated for other anomalies and a routine bronchogram should be a part of the clinical study.

Summary

An unusual case of Kartagener's syndrome was associated with lymphosarcoma of the small intestine in a 69-year-old man. Of 110 cases of Kartagener's syndrome heretofore reported, 35% do not have clear-cut evidence of bronchiectasis, and after reviewing several theoretical possibilities no definite final statement can be made regarding the pathogenesis of bronchiectasis. The lymphosarcoma occurring with Kartagener's syndrome has no likely etiological relationship.

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SPECIAL ARTICLE

SMOKING AND LUNG CANCER

A STATEMENT OF THE PUBLIC HEALTH SERVICE

Leroy E. Burney, M.D., Washington, D. C.

The Public Health Service is deeply concerned with the increasing death rate from lung cancer in the United States and in other parts of the world. Cancer of the lung is increasing more rapidly and causing more deaths than any other form of cancer in the adult male population. In the United States, the death rate from lung cancer among white men (age-adjusted) was 3.8 per 100,000 population in 1930; by 1956, the rate had risen to 31.0,[1] and more than 29,000 persons died of lung cancer in that year (fig. 1, table 1). A rising death rate of this magnitude arrests the attention of every physician, private practitioner and public health officer alike.

Many investigators have indicted cigarette smoking as responsible in large part for the increasing lung cancer death rate. Others have denied this, saying that increased volumes of automobile exhaust fumes and industrial vapors polluting the air are largely responsible for the causation of lung cancer.[2] The possibility that there are other factors yet unknown has also been suggested.

Two years ago I made the following statement: ". . . The Public Health Service feels the weight of the evidence is increasingly pointing in one direction: that excessive smoking is one of the causative factors in lung cancer." [3] Our belief then was based on reports that had been accumulating for more than 30 years. Since 1957, additional studies, some from our own staff, have contributed new information. I wish, in this paper, to review the data in those publications the Public Health Service has felt to be of particular value and to give our interpretation of the material presented.

The Smoking Hypothesis

In their classic study in 1928, Lombard and Doering [4] noted an association between heavy smoking and buccal cancer. Later, examination of time trends in mortality showed that the death rate from lung cancer was rapidly increasing. This immediately raised the question of a possible association of smoking with bronchial malignancy. Many studies [5] in different countries showed a higher proportion of smokers in lung cancer groups than in control groups.

Lombard and Snegireff.—The latest paper [6] in the Massachusetts studies on lung cancer and smoking deserves particular mention. The documen[illegible] each case is unusually thorough, covering a [illegible] range of factors. An extensive series of contro[illegible] was subjected to the same scrutiny. In a series of patients known to have died of lung cancer, four variables showed significant correlation and association: frequent or chronic respiratory conditions, heavy cigarette smoking, heavy consumption of alcohol, and outdoor work. Of these four variables, heavy cigarette smoking had by far the strongest relationship to lung cancer. "About four-fifths of the persons with lung cancer were heavy cigarette smokers (more than 9,125 packages), . . . about one-third had frequent or chronic respiratory conditions, about one-fifth were engaged in outdoor occupations, and about one-seventh were users of alcohol in excessive amounts."

However, there was criticism of the retrospective (historical) method, on which this paper and the earlier ones were based, as being subject to unavoidable bias. The following three studies, recently published, were designed therefore with a prospective (continuing) approach. Doll and Hill [7] reported from England, Hammond and Horn [8] for the American Cancer Society, and Dorn [9] from the National Cancer Institute of the Public Health Service (fig. 2 and 3).

Doll and Hill.—The Doll and Hill study [7] is a continuing analysis of 40,701 British physicians. Among male physicians 35 years of age and over, in the initial four and one-half years of observation, 1,714 deaths have occurred, including 84 from lung cancer. Deaths from lung cancer increased steadily with increasing amounts smoked; for nonsmokers the age-adjusted death rate was 7 per 100,000 of this population; for light smokers, 47; for moderate smokers, 86; and for heavy smokers (more than 25 cigarettes daily), 166. Giving up smoking reduced the susceptibility of a smoker to subsequent development of lung cancer. The decrease was greatest in those who had given up the habit for a decade or more. Those who continued to smoke more than 25 cigarettes daily from the beginning of the study had a mortality from lung

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Surgeon General, United States Public Health Service.

cancer nearly 40 times that of the nonsmokers. Pipe smoking was associated with lung cancer to a lesser degree than was cigarette smoking.

Hammond and Horn.—Hammond and Horn [8] have been conducting a longitudinal study of 187,783 white men aged 50 to 69. Analyses with regard to lung cancer in this age group at the end of 44 months support the findings of Doll and Hill. The 32,392 men who never smoked had an age-adjusted death rate from all types of lung cancer of 12.8 per 100,000 man-years. On the other hand the 63,332 men who gave a history of smoking cigarettes exclusively showed an age-adjusted death rate from this cancer of 127.2, a ratio of 10 to 1.

TABLE 1.—*Cancer Death Rates* per 100,000 White Men, by Specified Sites and Selected Years, 1930-1956*

Cancer Site	1930	1935	1940	Year 1945	1950	1955	1956
Stomach	33.8	31.5	27.8	24.9	20.3	16.2	16.1
Intestine	11.1	12.9	14.6	16.2	14.7	14.8	15.3
Rectum	6.3	7.6	8.8	8.8	8.3	7.8	7.7
Lung, trachea, and bronchus	3.8	6.5	10.2	14.2	20.8	28.9	31.0
Es[illegible]	3.3	3.1	3.8	3.8	3.9	3.7	3.8
[illegible]	4.6	4.6	4.2	3.5	2.9	2.7	2.7

[illegible]adjusted to the United States 1950 white male population.[47]

This study of Hammond and Horn is of particular interest since the reports of the individual deaths due to lung cancer were carefully checked and in most cases verified by microscopic diagnosis. The tumor deaths proved by tissue section constituted what the authors called the "well-established cases," on which further detailed studies were made. Adenocarcinoma of the lung was excluded from this group and treated separately because of the small number of cases (32) and also because of the general feeling that adenocarcinoma may be less associated with smoking than are other forms. Table 2 summarizes much of the Hammond and Horn study.

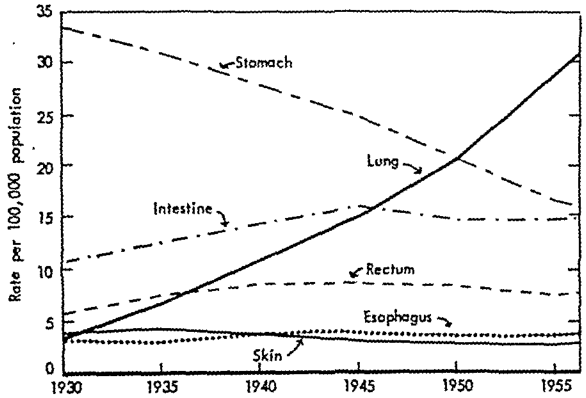

Fig. 1.—Trend in age-adjusted cancer death rates among white men, for specified sites and years, 1930-1956.[22]

Within the group of "well-established cases" the difference in death rates between the nonsmoker and the heavy smoker was striking, the ratio being 64 to 1. For those who had previously smoked cigarettes but had stopped the death rate was significantly reduced, and, as the period without smoking lengthened, the death rate became progressively lower, although it never reached the rate of those who had never smoked (fig. 3).

Dorn.—The Dorn study population [9] consisted of 249,000 U. S. government life insurance policy holders. At the end of two and one-half years of this continuing study there had been 7,382 deaths in the group. The increased proportion of deaths from any cause among the smokers as compared with the nonsmokers was greatest for cancer of the lung. The death rate from this malignancy among regular smokers of cigarettes was about 10 times that in the nonsmoking group. Regular cigarette smokers who had stopped smoking cigarettes before the study began in 1954 had a lower mortality than those who continued to smoke; however, this rate was still 30% greater than for nonsmokers.

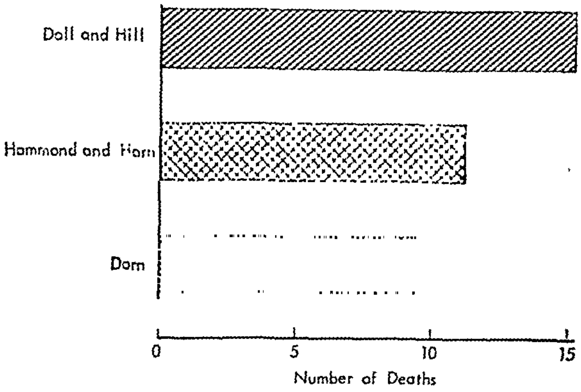

Fig. 2.—Number of deaths from lung cancer in smokers for each death in nonsmokers, by study.[48]

Criticism of the Smoking Hypothesis.—Not all investigators are in agreement with the conclusions reached by these researchers.

Berkson [10] noted that the data of Hammond and Horn and of Doll and Hill point not only to an association between smoking and lung cancer but also to a wide variety of diseases never presumed to have the same etiology as cancer. He suggests that some other explanation must be sought, stating, "1. The observed associations are 'spurious,' that is, they have no biological significance, but are the result of the interplay of various subtle and complicated 'biases.' The definitive variables, namely a history of smoking and the cause of death, are, as observations, subject to considerable error, and the samples, not having been obtained (or obtainable) by scientific sampling methods, are 'selected.' . . .

"2. The observed associations have a constitutional basis. Persons who are nonsmokers, or relatively light smokers, are the kind of people who are biologically self-protective, and biologically this is correlated with robustness in meeting mortal stress from disease generally.

"3. Smoking increases the 'rate of living' (Pearl), and smokers at a given age are, biologically, at an age older than their chronologic age. As a result, smokers (in particular, heavy smokers) are subject to the death rate of nonsmokers or relatively light smokers who are chronologically older. . . ."

Little[11] speaking for the scientific advisory board of the tobacco industry research committee, questioned "the existence of sufficient definitive evidence to establish a simple cause-and-effect explanation of the complex problem of lung cancer." He also said, "Many experiments on inhalation of cigarette smoke in animals have failed to produce a single cancer similar to the most prevalent type of lung cancer in humans."

Fisher[12] questioned whether the genetic factor can be dismissed. "There can therefore be little doubt that the genotype exercises a considerable influence on smoking and on the particular habit of smoking adopted . . . genotypically different groups would be expected to differ in cancer incidence. . . ." He quoted a study of the smoking habits of identical and fraternal twins in support of his thesis.

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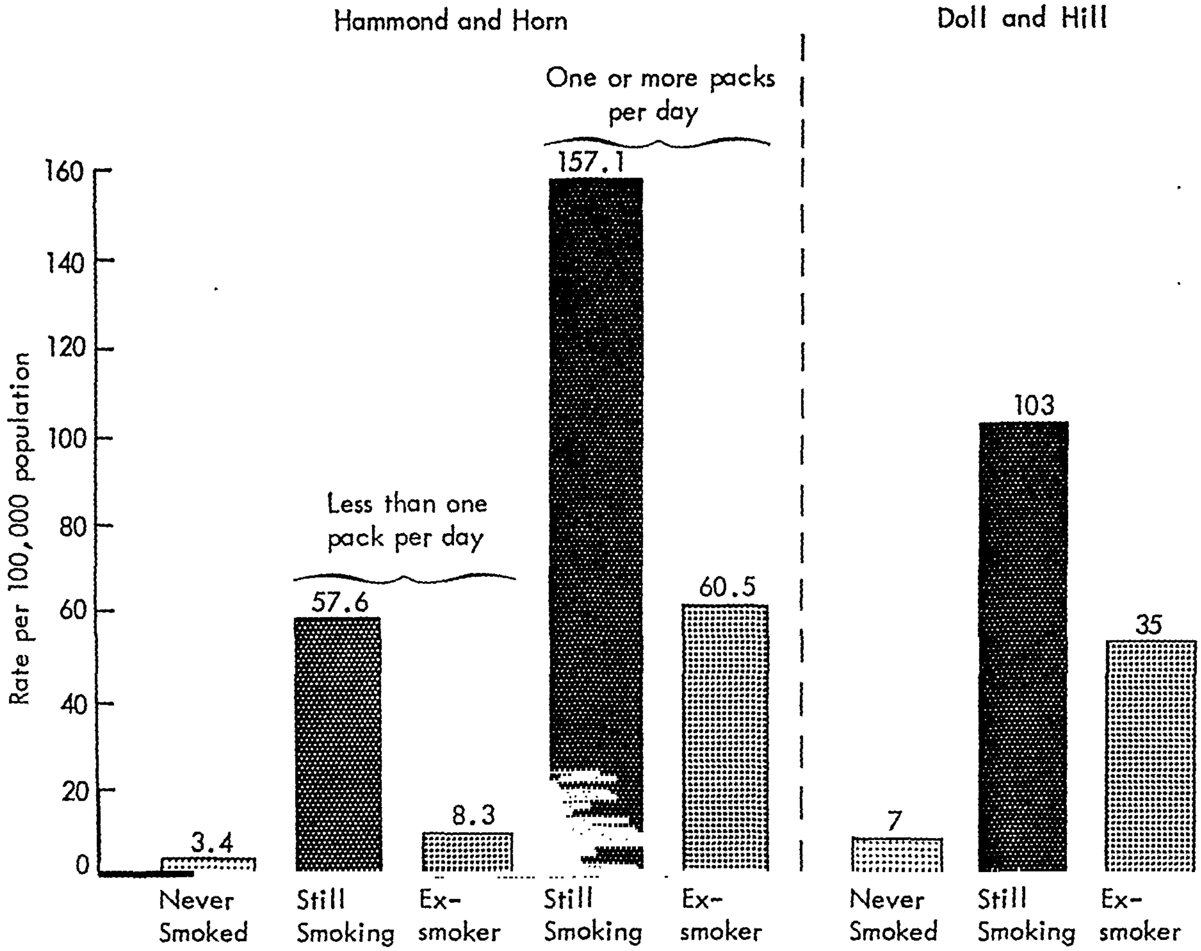

Fig. 3.—Age-adjusted lung cancer death rates for smokers, exsmokers (persons who had given up smoking for 10 years or more when interviewed), and nonsmokers, by study.[49]

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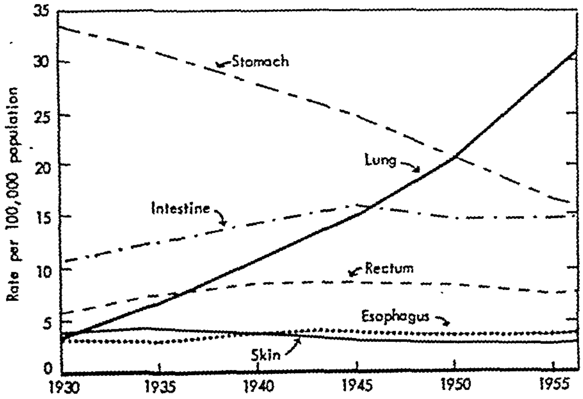

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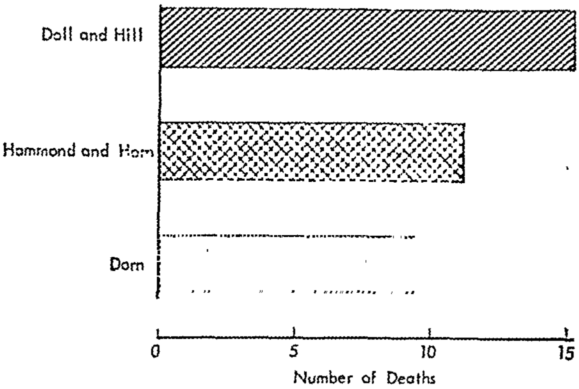

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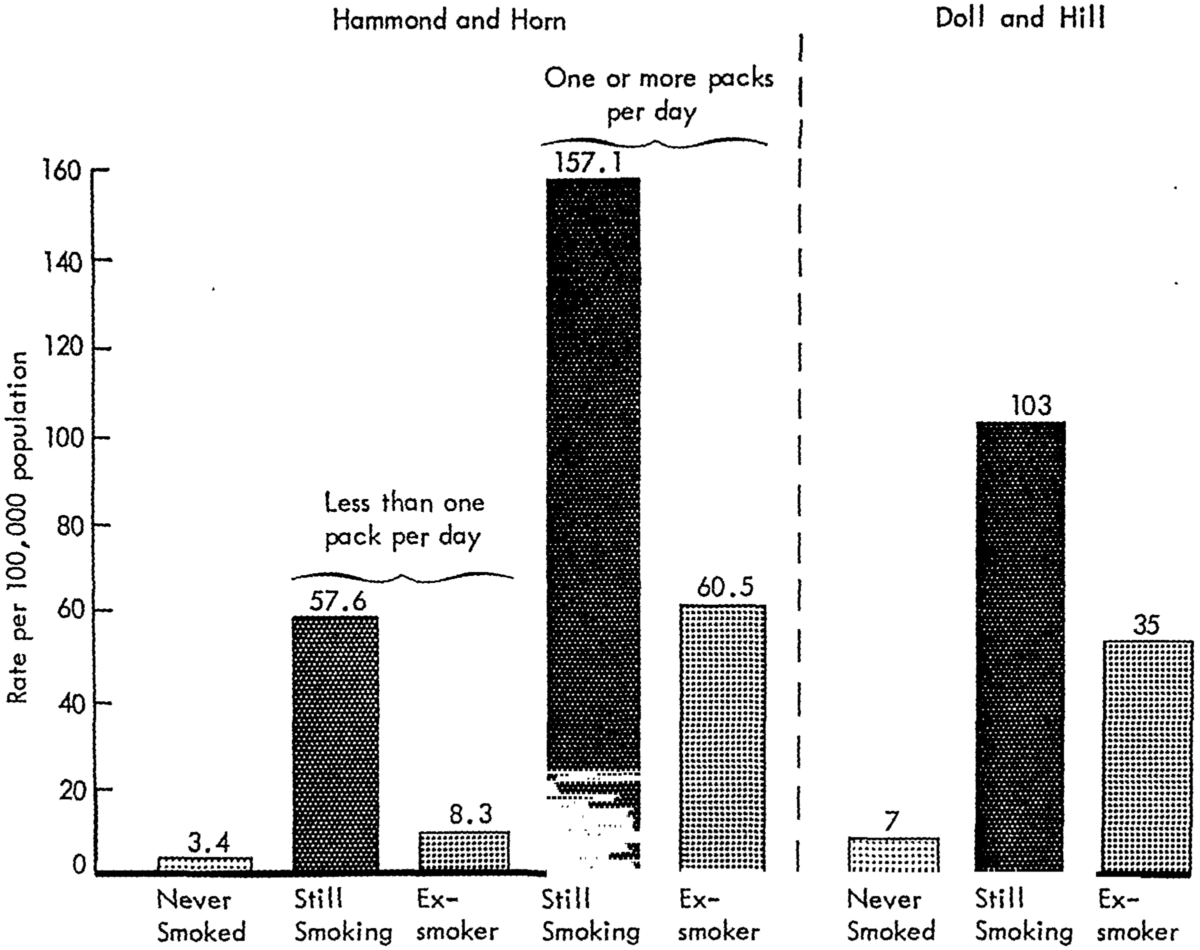

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selves encourage a desire to smoke." There may be secondary agents responsible in the "final efflorescence" of the disease in later years.

Herdan,[14] also in England, noted that death rates from tuberculosis and lung cancer seem bound together as a constant. As one has gone down the other has risen, so that the "probability that a person should die of either respiratory tuberculosis or C.L. [cancer of the lung] remains sensibly constant in the population." He believes that it is the antibiotic therapy of tuberculosis "resulting in the reduction of the combined mortality of males and females due to pneumonia and tuberculosis of the lung, which is responsible for bringing to the fore a disease which has its roots, partly at least, in the genetical make-up of man."

Table 2.—*Number of Deaths and Age-Standardized Death Rates* from Lung Cancer by Smoking Habits*†

	Deaths					
	All Cases		Well-Established Cases (Excluding Adenocarcinoma)		Adenocarcinoma	
1. Smoking Habits	No.	Rate	No.	Rate	No.	Rate
Never smoked	15	12.8	4	3.4	2	1.8
Occasional only	8	19.2	5	11.9	1	2.3
Cigars only	7	13.1	6	11.4	1	1.7
Pipes only	18	38.5	13	28.9	2	4.4
Cigars and pipes	3	7.3	2	4.9	0	...
Cigarettes and other	148	97.7	103	67.0	12	7.3
Cigarettes only	249	127.2	162	78.6	14	6.1
Total	448	68.0	295	44.5	32	4.7
2. *Current Daily Cigarette Smoking*‡						
Never smoked	15	12.8	4	3.4	2	1.8
Less than ½ pack	24	95.2	13	51.4	1	3.3
½-1 pack	84	107.8	50	59.3	5	5.1
1-2 packs	90	229.2	60	143.9	7	11.6
2+ packs	27	261.2	22	217.3	0	...

* Death rate per 100,000 man-years standardized to the age distribution of the white male population of the United States as of July, 1954.
† Data from Hammond and Horn.[8b]
‡ History of cigarette smoking only.

Supporting Opinions.—On the other hand, two groups of equally prominent authorities have come to an opposite conclusion. In June, 1956, the American Cancer Society, the American Heart Association, the National Cancer Institute, and the National Heart Institute, by joint action, organized the Study Group on Smoking and Health to review the effects of tobacco smoking on health and to recommend further needed research. After six two-day conferences, exhaustive examination of the literature, and discussion with scientists representing specialized areas of research concerned with the subject, the Study Group made this official statement[15]: "The sum total of scientific evidence establishes beyond reasonable doubt that cigarette smoking is a causative factor in the rapidly increasing incidence of human epidermoid carcinoma of the lung."

The second group, the British Medical Research Council, in 1957 published the following conclusions.[16] "1. A very great increase has occurred during the past 25 years in the death rate from lung cancer—in Great Britain and other countries. 2. A relatively small number of the total cases can be attributed to specific industrial hazards. 3. A proportion of cases, the exact extent of which cannot yet be defined, may be due to atmospheric pollution. 4. Evidence from many investigations in different countries indicates that a major part of the increase is associated with tobacco smoking, particularly in the form of cigarettes. In the opinion of the Council, the most reasonable interpretation of this evidence is that the relationship is one of direct cause and effect. 5. The identification of several carcinogenic substances in tobacco smoke provides a rational basis for such a causal relationship."

Other Factors

Since carcinoma of the lung is a disease that also occurs in nonsmokers, it is evident that factors other than tobacco contribute to its etiology. The major exogenous factors are air pollution and occupational exposure to carcinogens. The latter accounts for only a small percentage of lung cancer deaths.

Air Pollution.—Air pollution may be the "urban factor" which would help explain the higher death rate from lung cancer in urban as compared with rural areas (fig. 4).[17] The major sources of air pollution are exhaust products of gasoline and diesel engines, incomplete combustion products of petroleum and coal, many asphalt and bituminous products used in construction and road paving, and certain industrial effluents. The carcinogenic substances contained in these pollutants include polycyclic aromatic hydrocarbons such as 3,4 benzpyrene, 3,4 benzfluoranthene, some aliphatic oxides, and various inorganic compounds.[18] With the exception of coal all sources of air pollution have increased in recent years and therefore could be

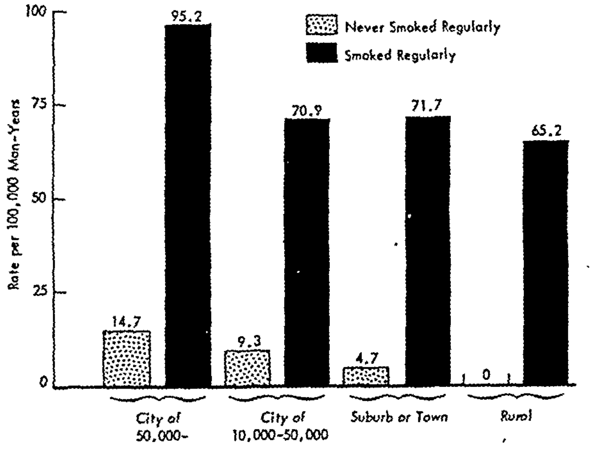

Fig. 4.—Age-adjusted lung cancer death rates for cigarette smokers and nonsmokers—urban-rural comparison (based on data from Hammond and Horn[8]).

environmental factors contributing to the rise in lung cancer (fig. 5).[19] There are also noncarcinogenic pollutants which are irritants and may affect the body's defense mechanism against inhaled carcinogens.[18]

Socioeconomic Status.—Some investigators [20] have found that low socioeconomic groups have an increased incidence of lung cancer. However, the low income group, by economic necessity, is apt to live near industrial centers where the air is more heavily contaminated with pollutants and airborne carcinogens than it is in peripheral residential areas. It is also true that the low socioeconomic group, as a whole, receives less adequate medical care and lives in a less hygienic environment than the more fortunate portion of society. Thus, it is difficult to measure any direct effect of socioeconomic factors alone.

Lower Mortality in Women.—Until 1926 lung cancer death rates among men and women in Massachusetts [21] (and, presumably, in the rest of the United States), were approximately equal. As lung cancer rapidly increased, its distribution between the sexes changed. In 1956, in both Massachusetts and the United States, the mortality in men was more than five times that in women.[22] This difference is not easily explained. There may be a true sex difference in susceptibility to the causes of increase in lung cancer, but the data are not conclusive.[5c]

Studies of apparent differences in smoking habits also have not accounted adequately for the variation in death rates between men and women. But there is conclusive evidence [5e] that nonsmoking women have about the same lung cancer death rate as nonsmoking men; that among women, the light smoker carries a risk of lung cancer twice that of the nonsmoker; and for the woman smoking more than one pack a day, the hazard is five times greater.

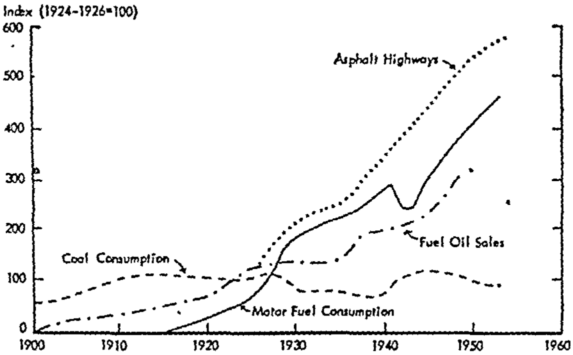

Fig. 5.—Selected environmental factors—trends for United States, 1900-1953 (adapted from Hammond[19]).

Physical Factors—Pipe and Cigar Smoking.—Hammond and Horn [8b] have shown that a person who smokes cigarettes has almost three times the risk of dying from lung cancer as the pipe smoker (fig. 6) and seven times that of the cigar smoker. It is possible that this relatively favorable status of pipe or cigar smokers may be due to the more adverse physical characteristics of cigarette smoke. Cigarettes burn at considerably higher temperatures than pipes or cigars.[23] Undoubtedly, too, deep inhalation of smoke is associated almost entirely with cigarette smoking.[24] Others [25] maintain that the lower death rates of persons who do not smoke cigarettes exclusively merely reflect their less extensive use of cigarettes.

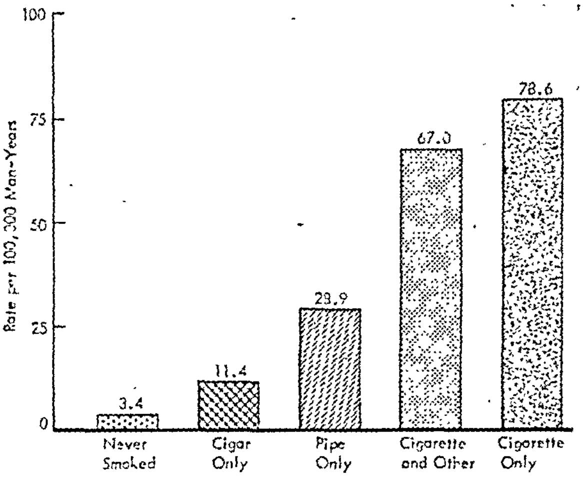

Fig. 6.—Age-adjusted lung cancer death rates by type of smoking (data from Hammond and Horn[8]).

A Concept of Pathogenesis of Lung Cancer

The association between the use of tobacco and buccal and lung cancer has been supported largely by statistical evidence until relatively recently. This in itself has seemed conclusive to many investigators, although the mechanism of cancer growth in the lung has never been demonstrated. If the smoking hypothesis is valid, it should be possible to show a sequence of events, started by cigarette smoke, which leads to the development of lung cancer. The same course could be initiated by the inhalation of carcinogens from polluted air. Several recent investigations lend support to such a concept of pathogenesis. It should be noted that this concept is theoretical, for the full course from causative agent to final tumor is not known in man. Furthermore, the statistical and experimental association between smoking and lung cancer applies essentially to the epidermoid type. The incidence of adenocarcinoma and undifferentiated carcinoma of the lung has changed little.[26]

Carcinogenic Substances.—It has long been known that certain polycyclic hydrocarbons are carcinogenic for animals and man. Those present in the tobacco leaf are fragmented at the burning temperature of the cigarette into incomplete combustion products and are included in the tar portion of the smoke. Wynder [27] has shown that cigarette tar produces cutaneous papillomas and carcinomas when applied for prolonged periods to the skins of laboratory animals. Confirmation of these studies has been reported from other laboratories.[28] There is little doubt that benzpyrene and other carcinogenic hydrocarbons found in soot are responsible for the classic human example of occupational cancer, Pott's epidermoid carcinoma of the scrotum in chimney sweeps. Cooper[29] in 1955 first demonstrated the presence of 3,4 benzpyrene in cigarette smoke. Benzpyrene is probably not the only carcinogen involved.[30]

Absorption by Cells.—Mellors[31] demonstrated that cells can absorb carcinogenic substances. When he gently scraped human squamous epithelial cells from the buccal mucosa and placed them in millionfold dilutions of cigarette tars, these same cells became "stained" by the products of cigarette tars and fluoresced characteristically when examined with the fluorescent microscope.

The Flow of Mucus and Ciliary Action.—Robertson[32] has reported on the phagocytic action of histiocytes extruded into the lumen of the alveolus. Macklin[33] noted that the alveolus is the point at which inhaled smoke comes into intimate contact with the rich capillary bed of the lung. The phagocytes appear to move out of the alveoli, along with a thin, mucoid coating, until the ciliated areas of the sub-bronchioles are reached. By the propelling force of ciliary action the mucous blanket, laden with foreign particles such as insoluble tobacco tars, moves slowly toward the trachea. From the relatively great total area of the alveolar regions the mucous stream follows a steadily narrowing path to the hilar regions where, by comparison, the cross-sectional area of the large bronchi is very small. During this passage the mucous blanket apparently becomes thickened and less fluid. Thus, the mucus is funneled and concentrated, along with its adherent tars, into the hilar areas, where there are additional mechanical reasons for stasis.

Concentration.—Occurring normally in the hilar bronchi are the numerous apertures of emerging bronchioles and patchy islands of nonciliated epithelium. Hilding[34] produced deciliated areas by injuring the bronchial mucosa and showed that the flow of the mucous blanket hesitates at these deciliated areas. In his study of the bronchi of freshly killed calves both India ink and, again, smoke were introduced into the mucous stream and observed for varying periods. When foreign material struck either the normally nonciliated regions or the areas of injured cilia, the particles collected on the "upstream" side and lagged behind, remaining in contact with the bronchial epithelium for prolonged periods before being swept on. There is no report as yet of a similar study in man.

Autopsy Studies.—Auerbach and co-workers[35] reasoned that lungs of smokers should reveal both destructive lesions and precursors of malignant change in the epithelium of the tracheobronchial tree. Their conclusions are based on some 25,000 sections from autopsies of 117 patients in whom the authors found changes they described as basal cell hyperplasia, stratification, squamous metaplasia, and carcinoma in situ. The cellular changes showed a statistically significant, increasing gradation. Sixteen nonsmokers had the fewest abnormalities. A higher percentage of abnormal slides were noted in the 20 patients who had smoked less than one package of cigarettes a day. Still more atypical were the findings in 47 patients who had smoked more than one package a day. Thirty-four patients dying of bronchial cancer (all smokers) showed the greatest number of areas of cellular aberration.

The Concept of Pathogenesis.—Tars containing benzpyrene and probably other carcinogens present in cigarette smoke (or contaminated air) are absorbed by the cells of the respiratory tract, especially in the alveoli. Here these foreign particles are picked up by phagocytes and transported toward the trachea in the mucous blanket of the bronchi. En route, concentration occurs where the cilia of the bronchial mucosa are injured or absent, and the motion of the mucous blanket is stopped for appreciable lengths of time. During this period the carcinogens contained in "tar" particles and in the mucus are afforded prolonged contact with the underlying bronchial cells, which react by malignant change.

Experimental Proof.—Experimental proof of this concept, to date, has not been supplied. The ultimate experiment would produce in laboratory animals, by the same type of exposure that occurs in humans, the same type of terminal tumor, preferably through the same sequence of preliminary changes as has been postulated above.

Rockey and his associates[36] applied tobacco "tar" directly to the bronchial mucosa of dogs and found that within three to six weeks the tar-treated surfaces became granular and later developed wartlike elevations. In the study of Leuchtenberger and co-workers[37] mice were exposed to cigarette smoke and examined after varying periods, the longest being 200 days. In most animals the bronchial epithelium showed inflammation and simple and atypical basal cell hyperplasia. Passey[38] stated, however, "Our failure during the past five years [recorded in previous publications] to induce lung tumours in mice, rats, and hamsters by exposure to strong concentrations of cigarette smoke is a striking negative result."

The findings of such experiments, *in toto*, are inconclusive. Whether this is due to inherent difficulties of the experimental methods employed[39] or to the problem of adequate control,[38] or whether this represents a true negative is not apparent at present.

Future Possibilities for Prevention

There can be no doubt that a significant proportion of the increase in lung cancer is real. This rise has not been caused solely by improvements in diagnostic techniques, better reporting on death certificates, or an increase of older persons in the population.[40] If we accept as valid the sequence of pathological changes given above, the prevention of lung cancer, to a large extent, becomes possible. This will be accomplished if carcinogenic substances from any source can be kept out of the air inhaled into the lungs.

Use of Filter Tips.—Filter tip cigarettes, which accounted for 1.4% of the market in 1952, now constitute approximately 50%.[41] This suggests that both the public and the manufacturers are concerned that some avoidable toxic agent may be contained in the tobacco smoke. Because the public has widely accepted filtered cigarettes, it is necessary to examine the effectiveness of the filtration.

Present knowledge[42] indicates that is not possible to filter, selectively, specific components such as carcinogens. Since the evidence from both human and animal studies shows that the risk of developing cancers is related to the amount of exposure to tar, the problem is to design a filter that will permit the minimum flow of whole tobacco smoke to pass, consistent with smoking satisfaction. The filters presently in use do not eliminate, but merely reduce, the tar. It is questionable whether, from a health point of view, any so-called minimum exposure to such a hazard should be accepted.

Table 3 gives the status of filters today, as found in two recent independent studies.[43] In both studies cigarettes were smoked to a standard butt length, at a standard rate, volume, and duration of puff. Any reduction in tar content of the smoke is accomplished only if the consumer does not smoke more than formerly and if the manufacturers do not alter the tobacco selection, cut, or packing to counteract any deficiency in taste caused by the filter.

It has been shown also that, whereas the major portion of carcinogenic substances is present in the tar, others may be found in the paper of the cigarette or in the tobacco additives used.[44]

Tobacco Treatment.—The possibility exists, in theory at least, of treating the tobacco before it is packed into cigarettes so as to eliminate the hazard of cancer. In practice, however, this has not been demonstrated.

Air Filtration.—Most investigators agree that air pollutants probably contribute to the elevated lung cancer death rate. Cancer-producing agents are in the air we breathe. Cancer can be produced in animals, with use of concentrates of urban smog. The cancer death rate in the largest cities is twice as high as that in nonurban areas. The case is not yet proved, but the weight of evidence grows heavier as research progresses.

It should be possible to reduce the amount of noxious material being discharged into the atmosphere by industry and by internal combustion engines.[45] Most of the major cities in this country have well-established smoke-control programs. Industry has done much already to institute better methods of combustion in manufacturing processes and to develop means of extracting pollutants from smoke and vapors before they are discharged into the air. Automobile makers now have devices in the laboratory stage that show promise of controlling the exhaust pollutants produced by the new fuels and the modern high-compression automobile engine. Further study and effort are required, but marked reduction in the future of carcinogenic air contamination is technically and practically feasible.

Change in Smoking.—Approximately 60% of the men and 30% of the women in the United States over 18 years of age smoke cigarettes.[46] Slightly higher incidences are found in the United Kingdom.

Recently two persons on the staff of the Public Health Service contributed to a review of the important studies in this field, including, among other papers, those listed above as critical of the smoking hypothesis. The group of statisticians and epidemiologists reporting this study[24] recognized that "there are areas where more research is necessary" and that "no single cause accounts for all lung cancer." However, they concluded that "the magnitude of the excess lung cancer risk among cigarette smokers is so great that the results cannot be interpreted as arising from an indirect association of cigarette smoking with some other agent or characteristic." If cigarette smoke carries carcinogens, control of smoking, no matter how difficult it may be, becomes a major factor in prevention of bronchial carcinoma.

TABLE 3.—*Comparison of "Tar" from Filter-tip and Regular Cigarettes Smoked Under Standard Conditions*[41]

	"Tar" Obtained, Mg.	
Length of Cigarette	Filter	Nonfilter
Regular (70 mm.)	27 (3 brands)	36 (6 brands)
Long (80 mm.)	35 (10 brands)	38 (2 brands)
King (85 mm.)	35 (14 brands)	46 (4 brands)

Conclusions

It is a statutory responsibility of the Public Health Service to inform members of the medical profession and the public on all matters relating to important public health issues. The relationship between smoking and lung cancer constitutes such an issue and falls within this responsibility of the Public Health Service.

The Public Health Service believes that the following statements are justified by studies to date. 1. The weight of evidence at present implicates smoking as the principal etiological factor in the increased incidence of lung cancer. 2. Cigarette smoking particularly is associated with an increased chance of developing lung cancer. 3. Stopping cigarette smoking even after long exposure is beneficial. 4. No method of treating tobacco or filtering the smoke has been demonstrated to be effective in materially reducing or eliminating the hazard of lung cancer. 5. The nonsmoker has a lower incidence of lung cancer than the smoker in all controlled studies, whether analyzed in terms of rural areas, urban regions, industrial occupations, or sex. 6. Persons who have never smoked at all (cigarettes, cigars, or pipe) have the best chance of escaping lung cancer. 7. Unless the use of tobacco can be made safe, the individual person's risk of lung cancer can best be reduced by the elimination of smoking.

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VIRUSES AS CAUSES OF DISEASE IN MAN.—A recent count indicates that there are more than 50 different diseases of man which are known or believed to be induced by viruses. Although this is an impressive number, it is greatly overshadowed by the different viruses that can be recovered from human beings, a number that now stands at more than 150. Of these agents, some 30 are known to be associated with respiratory diseases, and a majority of the remainder may initiate infections in the respiratory tract, the outstanding portal of entry for viruses.—Frank L. Horsfall Jr., The J. Burns Amberson Lecture, The *American Review*, September, 1959.

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SOME NOTES CONCERNING ANGINA PECTORIS

GUEST EDITORIAL

Samuel A. Levine, M.D.

THE actual cause and location of the origin of anginal pain is still obscure. The customary explanation that it is due to the lack of oxygen is not altogether satisfying. It must be due to the presence of something. Is it a catabolite like lactic acid or some other irritant? Is the origin of the pain in the muscle, insufficiently supplied by blood, or does it arise in the nerve plexuses that are abundant in the adventitia of the coronary arteries? Is a coronary vessel in spasm or distended and impinging on these sensory nerves producing the pain? These questions have not as yet been answered.

The lack of oxygen has been regarded as an explanation of too many difficulties in medicine. There are many patients with marked congenital cyanosis who have no angina and no congestive failure. They have constant relative anoxemia of the heart and other tissues of the body. Furthermore, patients with severe adrenal cortical hypofunction (Addison's disease) or myxedema may have a decreased cardiac output so that all organs, including the heart, receive a lessened amount of oxygen and yet show no evidence of angina or congestive failure.

As far as anginal pain is concerned it would appear that a localized lesion is an essential part of the difficulty. If one part of the heart is ischemic while the rest of the heart is normal or at least less involved, trouble develops. When the ventricle receives the impulse to contract, the weaker, less well nourished part has to keep pace with the stronger and more normal portions of the heart. When the force and vigor of contractions are too great, pain may be evoked in the relatively anoxemic portions. If the entire heart is feeble or equally involved in all its parts, as occurs in generalized cyanosis, myxedema, and adrenal cortical hypofunction, no pain results. The same is true of marked and even prolonged anemia. When anginal pain occurs in these conditions additional localized coronary sclerosis will generally be found. The conditions that evoke anginal pain are apt to be those that make the heart contract more vigorously. The reverse is also often true. Circumstances that decrease the strength and vigor of ventricular systole may decrease the tendency to angina.

Many years ago Fauteux, in the surgical laboratories of the Harvard Medical School, found that if both coronary arteries of a dog were simultaneously ligated ventricular fibrillation was much less likely to result than if only one was ligated. He also observed that, when one coronary artery was ligated but the proximal end was allowed to bleed, the tendency to ventricular fibrillation was decreased. Cardiac ischemia could not be the explanation of this type of sudden standstill of the heart. He thought that tension in one vessel was a factor in evoking the fatal arrhythmia. This also emphasizes the importance of localized lesions or abnormalities of the heart. This concept is in line with the idea of Beck and co-workers when they speak of the electrical imbalance of the heart as being responsible for sudden death that so commonly occurs in coronary cases.

It may be of interest to recall certain clinical correlations. Before the discovery of liver as a cure for pernicious anemia, patients with pernicious (Addison's) anemia showed the smoothest kind of arteries of any group of adults over 60 years of age who were examined post mortem. Angina pectoris and coronary thrombosis were extremely rare in these patients. Now, in similar cases when the anemia is treated effectively, angina and coronary thrombosis are common. Of course, the patients live longer and reach ages when arterial disease is more common. I doubt that that is the entire explanation. In parts of Peru where anemia is very prevalent, coronary thrombosis is much rarer in the same age decades than in those parts of the country where anemia is not endemic. Furthermore, generalized arteriosclerosis and coronary thrombosis are very extensive and very common in cases of polycythe-

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Remarks of moderator of panel on "Management of Intractable Angina Pectoris" at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

mia. Plethora and increased viscosity or turgidity of the blood must play important roles in the production of coronary thrombosis, and I wonder whether development of a mild chronic anemia might not be of value for certain vulnerable persons.

During a fluoroscopic examination of a patient who has both hyperthyroidism and angina one sees a very agile and hyperactive cardiac beat. After appropriate treatment, when a euthyroid status has been attained, the heart beats less vigorously and anginal pain has disappeared. It is customary to explain this improvement on the premise that the work of the heart has been decreased. The problem of supply and demand as far as the heart is concerned is thought to have been altered favorably. What has been overlooked is that not only has the cardiac output and work of the heart been decreased by this effective treatment but the supply of nutrition to the heart muscle through the coronary arteries has also been decreased. In other words, both demand and supply have been decreased. Either there must be some differential effect or some other mechanism must be involved. May it not be that the improvement is largely due to a lessening of the vigor of systole? The weakened or affected part of the ventricle is now not driven as hard with the basal metabolism +5% as when it was +50%. Now, when there is an increase in the work of the heart, the healthy or healthier portions of the heart increase their blood flow, while the sclerotic vessels fail to do so, but differential effect on the two portions is not as great as before.

Another circumstance in which it seems that weakening of the heartbeat may lessen anginal pain is the occasional disappearance of angina pectoris with the development of congestive failure. This can at times be ascribed to the fact that with heart failure the patient is unable to walk as briskly as before or as a result of dyspnea or weakness he cannot perform those efforts that formerly evoked pain. There are instances where such an explanation does not appear to be adequate. Pain at rest may disappear with congestive failure only to reappear as the failure improves. One may be hard pressed to decide which is preferable, more dyspnea and less pain or more pain and less dyspnea. A somewhat similar dichotomy of symptoms is present when one administers thyroid preparations to a patient with myxedema and angina; i. e., whether to choose more pain and less lethargy or the reverse.

Another clinical observation may have some bearing on this problem. At least it brings up challenging questions. When a patient develops anginal pain while recumbent, he will almost always want to sit up or stand upright. He has learned that the discomfort will be greater and last longer if he continues to lie down. The explanation of these observations is not altogether clear. There may be two mechanisms involved. In the upright position there is less venous return to the right side of the heart and therefore less output from the left ventricle. Secondly, with the trunk or the whole body upright the effect of gravity is helpful in moving fluid blood down the aorta. This might readily enable the left ventricle to put out its quota of blood with a less vigorous contraction. Here again, a weaker systole may be responsible for a lessening of anginal pain.

In this discussion no inference is to be drawn that it is desirable to weaken the heart in order to lessen the degree of angina. The purpose is to explore the possible mechanisms in the production of anginal pain. The final value of any therapeutic procedure will always depend on the results obtained on the functions of the entire body, physical and mental.

There is one surgical inference to be drawn from this concept of the mechanism of anginal pain. If one small artery supplying the lateral aspect of the left foot is narrowed or occluded by arteriosclerosis and produces pain on walking, it will do no good if an arterial graft is made that improves the circulation to a different part of the limb but does not improve the part that caused the pain. If the ailing part is involved in the act of walking, the patient's entire leg may be stronger after the operation, but now with the more vigorous stride the pain in the unimproved portion may be more easily evoked. The same mechanism may be applicable to operations on the heart. If additional blood supply is brought in by any means, such as the use of irritants like talc or asbestos or by endarterectomy, anginal pain could be alleviated only if the ailing part were improved. It is conceivable that, although a part of the ventricle might actually have been helped (increased blood flow) so that the vigor of systolic contraction has increased, the anginal pain might have worsened. If the vessel that was the main cause of the pain was not improved or was not helped sufficiently, the increased strength of the other portions of the heart might actually increase the severity of anginal pain. If this concept is valid it would explain why some procedures may help some patients with coronary disease and not others.

I might digress for a moment on a somewhat similar point of view as it applies to congestive failure. If the right ventricle expels one drop more per beat than the left, in a few hours several hundred cubic centimeters of excess blood will be present in the lungs, with resultant pulmonary edema. If the right ventricle delivers one drop less per beat than the left, venous congestion and hepatic engorgement will result in a few hours. One side of the heart cannot outdo the other side for more than short intervals. On the other hand, if both ventricles expel exactly one or two teaspoonfuls more or less per beat than normal no congestive failure develops, either venous or pulmonary. If the output is decreased, as in myxedema, the patient may merely feel weak. If it is increased as in hyperthyroidism he may feel warm and hyperactive but heart failure generally does not result. One may compare the situation to an automobile. If the tires are equally soft on both sides the car will drag and go slowly, but if the tire is flat on one side and firm on the other the car may turn over. The inference from this is that weakening the right ventricle or decreasing the return flow to the right side (phlebotomy) should and often does help pulmonary edema. Furthermore, if acute pulmonary congestion is not due to ventricular weakness (as often is true in cases of mitral stenosis with normal sinus rhythm) digitalis therapy should not be of much help. This also often proves to be true. Under these circumstances, the right ventricle is too efficient or too rapid and expels more blood than can be delivered through the stenosed mitral valve. It has long been known that in such cases attacks of pulmonary edema may disappear as the right ventricle weakens and fails. The patient may now have less dyspnea with a greater tendency to hepatic engorgement, ascites, and peripheral pitting edema. The two sides of the heart must work in unison and at times weakening one side is helpful in its total effect. This concept also explains why patients with mitral stenosis who also have tricuspid stenosis have comparatively less dyspnea and less tendency to attacks of pulmonary edema than those with mitral stenosis alone.

Another peculiarity of angina is the frequent lack of correlation between the work of the heart and the development of pain. It is common knowledge that in many instances a certain amount of physical effort will generally evoke an attack. Cases are often readily calibrated in the sense that about the same number of steps will repeatedly bring on the attack. What is more difficult to understand is that some patients can do a great deal of physical work at times without difficulty and yet not be able to walk one block up a slight incline. Many men are able to do strenuous physical work indoors during their daily occupation and yet cannot walk one block to the street car out of doors. Or a golfer who must take a glyceryl trinitrate tablet on going to the first hole may have no more trouble the rest of the game. Patients may have an attack repeatedly under the same circumstances, such as going to the garage or walking a short distance to the train or shaving in the morning, and have no spells doing much more strenuous things at other times. There is much about all this that makes one think of a conditioned reflex. The number of foot-pounds of work is not the whole story.

I would like to call attention to the diagnostic value and occasionally the therapeutic value as well of carotid sinus stimulation. I have found that when the test is carried out properly it is safe and often diagnostically decisive. If the patient is having spontaneous anginal pain and carotid sinus massage is applied and the heart slows considerably, the pain will lessen or disappear in seconds. Inasmuch as the interpretation of the test rests on the subjective sensation, the physician must ask a misleading question. After the manipulation is over the question is put: "Is the discomfort you had a few seconds ago worse since I touched your neck?" If the pain was anginal in origin and the heart slowed to a moderate or a marked degree the patient will almost invariably reply, "no, it is gone" or "no, it is lessening." No such relief occurs if the heart rate had not been slowed. While the explanation of this almost instant relief is obscure, it probably is due to a washing away of the irritating catabolite during the longer diastolic intervals.

One of the few points about angina that appears certain is the strong familial hereditary factor. There are other factors such as diet, obesity, and stress and strain, but how important they may be remains debatable. Many young men who die of coronary thrombosis show a localized lesion in one part of a coronary artery post mortem and little, if any, arteriosclerosis elsewhere in the body. If an elevated blood cholesterol or uric acid level were to blame for this arterial lesion why did it pick out one part of one coronary vessel and spare the rest of the vascular tree? If a patient had jaundice of one finger one would look especially to the blood vessels of that finger for a likely explanation of the localization of the jaundice to that part of the body. The obvious inference is that detailed study must be made of the variations in the architectural anatomy and motion and function of the coronary arteries in different normal persons. A very slightly different twist of a vessel here or a more acute angle at another point may determine whether it will take 40 or 70 years of torsion and contraction for the vessel to show evidence of disease. Such careful studies may prove illuminating and explain why there are families with long-lived coronary vessels and others with short-lived vessels.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Few physicians, if any, would fail to choose medicine as a career if again given the opportunity. Most of us would select medicine because of our gratifying experiences in our practices, our research, our teaching, or our specialized services. In addition, we would see the new and vast opportunities now available to young physicians.

Students, however, must choose a career "in the dark"; they usually have not had previous experiences in their selected field; and, unfortunately, too many of them do not see the abundant opportunities now available in a medical career. Many "potential" medical students are attracted elsewhere by the drama and the assured wages of various scientific fields and the recruiting programs of industry.

Despite the keen competition by others for scientific brains, medicine must graduate more and more medical students to keep pace with our nation's growth. However, we cannot merely say we need more medical school graduates. We must find the talented students with medical interests. We must convince them that there are "new worlds to conquer" in medicine, too. We must show them that although medicine is one of the oldest professions, there is always a newness and warmth about it that makes the life of a physician most rewarding and satisfying.

You and I must lend a hand in discovering future physicians and in promoting a medical career for these men and women. Indeed, I firmly believe that we have an obligation to all patients, medical schools, and our profession to uncover the best students to carry on the great traditions of medical care and advancement.

I hope that you share my concern over the steady decline in the number of applicants for first-year positions available in medical schools. Ten years ago there were as many as 3.47 applicants for every opening. Now that rate is down to 1.87, and it may drop further in 1960.

Of equal importance is the fact that the percentage of "A" students among college graduates enrolling in medical schools has dropped from 40% in 1950-1951 to 16% in 1958-1959. This is a significant decrease and is coincidental with the decline in the number of applicants for medical school. As a result of this decline in number of students with "A" college grades, there has been an increase in the number of medical students who have had "B" college grades. However, it is entirely possible that even the percentage of first-year medical students with "B" grades might decrease. This possibility should concern all of us.

On the brighter side, we do know that the size of college graduating classes is going to rise in the immediate years ahead. This will be due to the higher percentage of college attendance and the high birth rates in the 1940's. From these graduating classes there could be an adequate pool of medical school applicants.

I believe that each of us should take a personal interest in one or more potential candidates for the medical profession. We might counsel and guide these students much as a member of the clergy does for a young person who is suited for the ministry.

There is a welcome place in our nation's medical schools and in our profession for the talented student. I hope that you will help him seek and find that place.

Louis M. Orr, M.D.
Orlando, Fla.

MEDICAL NEWS

CALIFORNIA

Physical Examinations for Hospital Staff.—On Aug. 12 the Culver City Hospital instituted a program of physical examinations for all professional members of the staff. This program includes a complete physical examination, x-ray of the chest, electrocardiographic study, complete blood count, urine analysis, serology, blood sugar and cholesterol estimation. Where chief complaints warrant, additional laboratory and x-ray studies are conducted. Physical and laboratory procedures, along with any additional studies, are free. According to the examining doctors, at least 20% of the physicians undergoing these examinations have additional x-ray and laboratory examinations. As of Oct. 21, 50% of the staff members availed themselves of the opportunity of these voluntary checkups. Chairman of the committee in charge of this program is Dr. Sidney Messer, Santa Monica.

DELAWARE

State Medical Election.—The officers of the Medical Society of Delaware are: president, Dr. James E. Marvil, Laurel; president-elect, Dr. Lemuel C. McGee, Wilmington; vice-president, Dr. Charles M. Moyer, Laurel; secretary, Dr. Norman L. Cannon, 1208 Delaware Ave., Wilmington; treasurer, Dr. Charles Levy, Wilmington; delegate to the A. M. A. (until December, 1961) Dr. H. Thomas McGuire, New Castle; alternate delegate to the A. M. A., Dr. Leslie M. Dobson, Milford; and executive secretary, Mr. Lawrence C. Morris Jr., 1925 Lovering Ave., Wilmington. The by-laws of the Medical Society of Delaware were amended this year to provide that officers shall take office at the annual meeting rather than on Jan. 1, which had been the custom.

GEORGIA

Governor's Commission on Aging Appointed.—Governor Ernest Vandiver has appointed a Commission on Aging to look into the problems relating to the older citizens of Georgia. The commission has been charged with the responsibility of representing the State of Georgia at the White House Conference on Aging in January, 1961. In addition, the commission will coordinate activities on aging in the state, conduct research in this field, encourage and promote the use of existing resources to meet needs throughout the state, and make recommendations to the governor on "courses of action relating to the problems of the aging and the aged." Dr. John T. Mauldin, Atlanta, representing the state at large, has been appointed chairman of the commission. Dr. John S. Atwater, Atlanta, Chairman of the Medical Association of Georgia Committee on Health Care of the Aging, will represent the association on the commission.

ILLINOIS

Rabies in Illinois.—The first case of rabies in a bat in Illinois was reported to the Evanston Department of Health on Thursday morning, Oct. 29. Dr. Edward Press, Evanston public health director, stated that the Evanston Health Department and Police Department and many other health departments have been particularly alert to the possibility of rabies in bats since the death from rabies on Sept. 6 of a 40-year-old farmer from Blue River, Wis. This was the second bat from Evanston sent during the past month to the State Health Department Laboratories in Chicago for examination regarding the presence of rabies. The first bat (which had bitten a cat that in turn scratched a woman) was found to be negative. The second bat was found to be positive for rabies following mouse inoculation tests, under the direction of Richard A. Morrissey, chief of the Virus Diseases and Research Bureau of the State Division of Laboratories. In this instance an 8-year-old girl had fallen from her bicycle in the northeast section of Evanston, accidentally landing directly on a brown bat which may have bitten her on the knee. The last two rabid animals in Evanston were a dog and an opossum in 1954. Edward C. Kheun, D.V.M., the Cook County rabies control officer, reports that there was one rabid animal this year in Cook County outside of Evanston. From Jan. 1 to Sept. 11 a total of 30 rabid animals were detected in the State of Illinois. These included 12 skunks, 1 raccoon, 2 foxes, 1 squirrel, 4 dogs, 4 cats, 5 cows, and 1 rat. As of Oct. 1, about 240 individuals had reported animal bites to the Evanston Health Department. Although cases of human rabies are rare as compared with other diseases, rabies is widespread in animals in the United States and in recent years has been on the increase. If any person is bitten by a warm-blooded animal he should contact his physician or a hospital immediately and then report the incident to the health department or police department or both. The animal involved should not be killed but

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

should be impounded for 10 days and carefully watched inasmuch as, if it can be shown that the animal is not rabid, the patients will be spared the pain and expense of the series of injections of vaccination that is required. The State Health Department provides antirabies vaccine to physicians through local health departments for use in patients where the possibility of contracting rabies exists.

Chicago

Dr. Wilburn Feted.—Dr. Homer V. Wilburn was honored in October at a testimonial dinner given by the Joint Negro Appeal of Chicago. Dr. Wilburn, 71, was feted "for his distinguished medical and civic career." He has been a physician for nearly 40 years and is a specialist in metabolic diseases. In 1942 he became medical director of Provident Hospital, where he is now honorary senior attending physician.

Dr. Dooley to Be Honored at Luncheon.—A luncheon in honor of Dr. Thomas A. Dooley, known for his work in behalf of the people living in the jungles of Laos, will be held Nov. 28 at the Sheraton Hotel, sponsored by Loyola University and the Catholic Action Federations. Dr. Dooley will speak about his efforts to provide health service throughout the underprivileged areas of the world. In his hospital in Laos, 36,000 patients were treated in the past year. Drugs, supplies, and surgical instruments were provided by American manufacturers. To further his work, Dr. Dooley founded Medical International Cooperation (MEDICO). In the past two years this organization has forwarded more than $500,000 worth of drugs to hospitals which it supports in Burma, Cambodia, French Africa, Haiti, Jordan, Laos, Pakistan, and Peru.

KANSAS

Clergymen Take Hospital Course.—An eight-week orientation course for ministers and theological students is in progress at the Osawatomie State Hospital, Osawatomie. The eight clergymen who have enrolled in the course which started Oct. 12 will meet at the hospital each Monday for eight weeks for an all-day session in psychiatric pastoral training. The course is under the supervision of hospital Chaplain Donald Hood who is accredited by the National Council for Clinical Training, Inc., New York, to conduct training programs for theological students and community clergy. The program is designed "to acquaint the clergymen with the treatment program of the Osawatomie Hospital and to help them better understand the pastoral problems of parishioners and patients." The sessions include lectures and films on mental illness and a course in "Psychiatric Syndrome" conducted by Dr. Edgar Jackson, staff psychiatrist. The clergymen participate in seminar groups for the discussion of pastoral problems and counseling, and visit patients.

MASSACHUSETTS

Lay Cornerstone for Research Building.—During the annual meeting of the Massachusetts Memorial Hospitals Medical and Surgical Society, cornerstone-laying ceremonies for Boston University's new 3-million-dollar medical research building, part of the Boston University–Massachusetts Memorial Hospital Medical Center, were held. Dr. Chester S. Keefer, of Boston, director of the Medical Center and former dean and director of the Boston University School of Medicine, presided at the ceremonies Oct. 21. President Harold C. Case of Boston University was a speaker. The new seven-story research building will house 45,000 square feet of research laboratory space. The sixth floor will be devoted to an animal laboratory, and each floor will include a conference room.

Students Receive Scholarship Aid.—Governor Foster Furcolo announced Nov. 4 that 262 students in medical, dental, and nursing schools have received scholarship aid totaling $57,130 from the Medical, Dental, and Nursing Scholarship Board. The board was created in August, 1957, by the Massachusetts Legislature. The awards announced Nov. 4 are the second group to win scholarships as a result of the legislation. In 1958, 192 students received aid, for a total of $50,000. Each recipient is attending the college of his or her choice anywhere in the United States. Seventy-one scholarships, valued at $21,500, were given to students attending 25 different medical schools. Sixty-five awards totaling $19,550 go to dental students attending 11 schools, while one hundred twenty-six awards worth $16,080 are for nursing students now enrolled in 44 different schools of nursing. The medical student awards average $303 each, with 56 awards of $250 and 15 awards of $500 being made. Applications for these awards were made available to all interested students who show "academic standing and financial need." The applications are sent to all medical, dental, and nursing schools in the Commonwealth for distribution. Plans are now being made for the 1960-1961 academic year, and applications will be mailed to all medical, dental, and nursing schools in Massachusetts.

MICHIGAN

Dr. Warren to Give Annual Lecture.—Dr. Shields Warren, Boston, will present the fourth annual Carl V. Weller Lecture to the Michigan Pathological Society at 5 p. m., Dec. 12, in the Reckham Building of the University of Michigan, Ann Arbor. Dr. Warren's topic will be "The Pathology of Ionizing Radiation." The lecture series, honoring the late professor of pathology at the University of Michigan Medical School, was established in 1956. Preceding the lecture the members of the Michigan Pathological Society will attend a slide seminar on "Interesting Problem Cases."

Hospital Staff Honors Dr. Connelly.—At the 12th annual Clinic Day at Bon Secours Hospital, Grosse Pointe, Dr. Richard C. Connelly, Detroit, was presented an "Award for Distinguished Service." A plaque given to Dr. Connelly on behalf of the Sisters of Bon Secours and the medical staff at a dinner, Oct. 21. Bon Secours Hospital was founded as a hospital for the care of the acutely ill 14 years ago and Dr. Connelly has been associated with the institution since this beginning.

Annual Reregistration for Physicians.—Beginning Jan. 1, 1960, there will be an annual reregistration fee of $5 for every doctor of medicine licensed under the Michigan Medical Practice Act, who is desirous of keeping his Michigan Medical license in force. Section four of the act reads in part as follows:

> Every person licensed under this act and wishing to continue in the practice of medicine, surgery, and midwifery in any of its branches in this State shall annually on or before January first re-register with the Board of Registration in Medicine on a form to be provided by said Board, but re-registration under this section shall not be required of a physician during the calendar year, in which he is originally licensed under Section 3 of this act. The re-registration form, to be signed by the applicant, shall contain his name, his residence address, the address at which he is engaged in practice, and such other identifying information as the board may require. A licensee who fails to re-register before January 1 shall be so notified by certified mail to his last known address, and until March 1 may re-register as above provided, except that the re-registration fee for the year shall be $10.00. The license of a licensee who has not re-registered before March 1 shall be considered suspended until such time as he shall re-register, at which time he may be reinstated by the board upon the payment of a re-registration fee of $10.00, and no further examination shall be required by the board as a condition to such reinstatement. When any person licensed under this act and practicing in this state shall change his place of residence in this State, or shall move out of the State, he shall, within 30 days after such change, so notify the board.

MINNESOTA

Dr. Myers Honored.—Dr. Jay Arthur Myers, professor emeritus of public health and internal medicine, University of Minnesota Medical School, Minneapolis, received the university's Outstanding Achievement Award Sept. 28. The award, conferred by Dr. Robert B. Howard, dean of the College of Medical Sciences, is given to former students of the university who "attain highest distinction in their chosen fields or in the area of public service."

MISSOURI

Exhibit of Dr. McComas Collection.—A collection of items once owned by or related to the career of the late Dr. Arthur Rochford McComas, Sturgeon, physician and University of Missouri alumnus, has been placed on display in the main corridor of the university Medical Sciences Building. The exhibit, open to the public, will remain on display until Dec. 1. Dr. McComas died in November, 1956. Last June the School of Medicine announced establishment of the Arthur Rochford McComas Memorial Medical History Essay Contest for students enrolled in the school. One of the items in the display is an amputation kit used by Dr. McComas, which was presented to him in 1919 by the late Dr. A. W. McAlester, who for years was dean of the University School of Medicine.

NEW JERSEY

Annual Seminar in Pathology.—The New Jersey Society of Pathologists, with the New Jersey State Department of Health cooperating, will hold its ninth annual slide seminar Dec. 5 at the Essex House, Newark. The moderator will be Dr. Hugh G. Grady, professor of pathology at Seton Hall Medical School, Jersey City. Microscopic slides and case histories were mailed out for tumors of the breast and various trophoblasts. Many out-of-state pathologists will attend. All physicians are invited. The annual seminar dinner will follow the meeting at the Essex House.

NEW MEXICO

Regional Meeting of Physicians.—The New Mexico regional meeting of the American College of Physicians will be held in Albuquerque, Dec. 5. The scientific sessions will be conducted at the Bernalillo County Health Department Building Auditorium. A luncheon meeting of the New Mexico Society of Internal Medicine will be held from noon to 2 p. m. Dr. Robert Friedenberg, Albuquerque, governor for New Mexico, will preside at the opening session. Dr. Karver L. Puestow, Madison, Wis., regent of the college will present, "Chronic Ulcerative Lesions of the Intestinal Tract" at the afternoon session and will give "Medicine Today in the Land of the People of the Book" at the dinner session, 7:30 p. m.

NEW YORK

Annual Meeting on Industrial Medicine.—The annual meeting of the New York State Society of Industrial Medicine, Inc., will take place at the New York University Club, 123 W. 43rd St., New York City, Tuesday, Dec. 1, 5 p. m. The program is as follows:

Workmen's Compensation is Rehabilitation, Col. Solomon E. Senior, chairman, Workmen's Compensation Board State of New York.
Current Developments in Malpractice Litigation, Mr. William F. Martin, counsel, Medical Society of the State of New York.
Discussion until 6:30 p. m.

For information, write Dr. Anthony A. Mira, director of the Bureau of Industrial Health and Workmen's Compensation, Medical Society of the State of New York, 750 Third Ave., New York 17.

Postgraduate Assembly in Anesthesiology.—The 13th annual Postgraduate Assembly in Anesthesiology will be held at the Hotel New Yorker, New

York City, Dec. 9-12. Among the speakers will be Dr. Seymour S. Kety, chief of the Laboratory of Clinical Sciences, National Institute of Mental Health, Bethesda, Md., who will preside at a symposium on cerebral circulation. Panels on the following subjects will be presented:

Problems of the Poor Risk Patient
Venous Mechanisms and Cardiac Output
Problems of Ventilation
Clinical Hypnosis
Vasopressors
Local Anesthetics

Luncheon conferences will be arranged and a closed circuit television program will feature new advances in anesthesiology. On the last day a "residents' program" will offer papers on the frontiers of anesthesiology. This meeting is sponsored by the New York State Society of Anesthesiologists, Inc. For information, write to the secretary, Dr. Edwin J. DePolo, 131 W. 11th St., New York 11.

New York City

Lectures to the Laity.—Dr. Paul D. White, Boston, spoke on newest advances in heart disease treatment and prevention as the New York Academy of Medicine's first of the season Laity Lectures, Nov. 4. The 25th annual Lectures to the Laity take "Frontiers of Medicine" as the theme of six lectures by leaders in medicine. On Nov. 18, "Cancer Research, Its Pattern" was given by Dr. John R. Heller, National Cancer Institute, Bethesda, Md. Other lectures are as follows:

Dec. 9—Hypnotism—Its Uses and Limitations, Dr. Lewis R. Wolberg, professor of psychiatry, New York Medical College.
Jan. 6—Tranquilizers and Stimulants—Their Use and Abuse, Dr. Francis J. Braceland, psychiatrist-in-chief, Institute of Living, Hartford, Conn.
Jan. 20—Narcotics Use by Teen-Age Boys, the Perspectives, Isidore Chein, Ph.D., professor of psychology, N. Y. U.
Feb. 3—Obesity, Prevention and Treatment, Dr. Herbert Pollack, N. Y. U. Postgraduate School of Medicine.

Personal.—Dr. Stanley Lesse, of the Columbia-Presbyterian Medical Center, was appointed editor-in-chief of the *American Journal of Psychotherapy*. The editorial office is at 15 W. 81st St., New York 24.——Chandler McCuskey Brooks, Ph.D., chairman, department of physiology, College of Medicine, Downstate Medical Center, State University of New York, was appointed to serve a three-year term on the selection committee for the senior research fellowship program of the National Institutes of Health, U. S. Public Health Service.——George Y. Shinowara, Ph.D., Columbus, Ohio, was appointed professor of pathology at the New York University College of Medicine and has assumed direction of a new laboratory set up in the NYU-Bellevue Medical Center to carry on his research in the study of blood, tissue proteins, and coagulation components. He will also be director of biochemistry for Bellevue Hospital and for New York University Hospital.——Dr. Robert Turell was invited by the Sociedade Brasileira de Proctologia to be their "honor guest" at their ninth congress, held in Porto Alegre Nov. 3-7. His topics were "Treatment of Massive Rectal Prolapse" and "Epidermoid Cancer of the Perianus and Anal Canal."

NORTH CAROLINA

Physicians Meeting in Chapel Hill.—On Thursday, Dec. 3, the 26th annual North Carolina regional meeting of the American College of Physicians will be held in Chapel Hill, with the University of North Carolina School of Medicine as host. Presentations by the department of medicine at the university are planned for 2 p. m. as follows:

The Effect of Varying Potassium Concentrations on the Electrical and Mechanical Activity of Isolated Hearts from Rats, Dr. Isaac M. Taylor.
Left-Sided Hemodynamic Studies During Surgical Closure of Patent Ductus Arteriosus, Dr. Thomas Gibson, Dr. Ernest Craige, and Dr. Richard M. Peters.
Salt Restrictions and Hyperplasia of the Zona Glomerculosa of the Rat, Dr. Margaret Newton and Dr. Louis G. Welt.
Enzymatic Changes in the Serum and Liver of Patients with Hepatic Disease, Dr. Oscar L. Sapp III, Dr. William G. Wysor Jr., Dr. Nathan A. Womack, and Dr. John T. Sessions Jr.

Honored guests at the meeting will be Dr. Howard P. Lewis, Portland, Ore., president of the college who will be dinner speaker, and Mr. Edward R. Loveland, executive secretary of the college. A clinical pathological conference is planned.

TENNESSEE

Dr. Alden Named Associate Dean.—Roland H. Alden, Ph.D., chief of the division of anatomy at the University of Tennessee Medical Units in Memphis since 1949, was named to the newly created position of associate dean of the Graduate School for Medical Sciences. Dr. Alden will begin his new duties Jan. 1, retaining his position as chief of the division of anatomy. He will be taking over a portion of the duties performed by Thomas P. Nash Jr., Ph.D., dean of the School of Biological Sciences.

UTAH

Report on Accident Rate.—The Utah State Department of Health reported that in the first six months of 1959 224 people died in accidents and 18,000 suffered injuries. The heaviest death toll resulted from traffic accidents with 84, followed by home accidents with 50, and public nonmotor vehicle accidents, such as falls, firearm accidents, and drownings accounted for 49 deaths. Traffic multiple-fatal accidents in which two or more persons were killed in the same accident accounted for 22 deaths. Out-of-state drivers were involved in 19% of the fatal accidents. One-third of the 96 drivers involved in the fatal accidents were 24 years of age or under. The 25-34 age group was next highest with 28 drivers involved. Home accidental deaths were largely due to falls, burns, choking, drowning, and firearms. Infant children and the aged were the most frequent victims. Salt Lake County recorded over half of the deaths in this classification. The death toll from accidents in Utah last year was 550.

GENERAL

Flying Physicians Meet in Dallas.—An ancillary meeting of the Flying Physicians Association, organized by the Texas chapter, will be held Thursday, Dec. 3, 12:45 p. m., at the Love Field Holiday Inn, Dallas. Transportation will be arranged for all members from the Memorial Auditorium where the general registration booth will be located. The program will consist of short papers on civilian defense and mobilization, specifically on participation of the Flying Physicians Association in programs on a local and state basis. For information, write Dr. George M. Boswell Jr., 364 B Casa Linda Plaza, Dallas 18, Texas.

Regional Meeting of Pharmaceutical Manufacturers.—The eastern regional meeting and annual award dinner for the Pharmaceutical Manufacturers Association will be held at the Waldorf-Astoria Hotel, New York City, Dec. 7-9. Sessions will be held Dec. 7-8 on production, foreign operations, marketing, and medical and scientific topics. The award presentation dinner, which will honor Dr. Cyril N. H. Long of Yale University School of Medicine, New Haven, Conn., winner of the 1959 P. M. A. Award, will be Dec. 8. A morning session on socioeconomic problems Dec. 9 will include speakers from Austria, England, Sweden, and Canada. For information, write the Pharmaceutical Manufacturers Association, 1411 K St., N. W., Washington 5, D. C.

Group Giving to Education Fund.—The National Fund for Medical Education announced that this Christmas medical schools will again benefit from a program of group giving, whereby the Carling Brewing Company of Cleveland in the name of its wholesalers will donate $12,000 to the fund, instead of spending that sum on individual presents for its 680 distributors. The contribution will be included in about 3 million dollars to be awarded this year to the medical schools by the fund in unrestricted grants. The corporate-giving plan was initiated last year by the Carling Brewing Company of Cleveland, with the cooperation of its distributors. The 1958 contribution totaled $10,000. The fund, founded in 1949 by Dwight D. Eisenhower, then Columbia University head, former President Hoover, James B. Conant, Ph.D., and other leading educators, channels contributions from industry to the medical schools. Since the first grants were made in 1951, it has distributed $18,668,946.

Chemical Society Establishes New Division.—A Division of Public, Professional, and Member Relations was established by the American Chemical Society to coordinate and expand the society's communications activities. It will be part of the headquarters staff of the ACS in Washington, D. C., and will report to the executive secretary, Mr. Alden H. Emery, Silver Spring, Md. The division will be in operation by Jan. 1, 1960. Mr. James H. Stack, managing editor of the ACS News Service since 1948, has been named director of the division. The new division also will have an Office of Professional and Government Relations. Creation of the division was authorized by the ACS board of directors after a four-year study of the society's communications needs by the board's committee on member and public relations.

Postgraduate Meeting in Mexico.—A clinical postgraduate program will be held Feb. 25-March 5 in Mexico City, sponsored jointly by the UCLA School of Medicine, University Extension, and the National School of Medicine, Mexico City. The 10-day program will present lectures by authorities from the two universities in the field of internal medicine, cardiology, dermatology and mycology, pediatrics, anesthesiology, general surgery, and traumatic surgery. Lectures and clinics will be held on weekday mornings, with the afternoons and weekends free. Special planes for the conference will leave from Los Angeles and Chicago. Conference enrollment will be limited; reservations will be made in the order in which applications are received. Information and applications may be obtained from the Department of Continuing Education in Medicine, UCLA Medical Center, Los Angeles 24 (BRadshaw 2-8911, Ext. 7114).

Meeting of Southern Surgeons.—The 71st annual session of the Southern Surgical Association will be held Dec. 8-10 at the Homestead, Hot Springs, Va. Dr. George G. Finney, Baltimore, will open the meeting with the presidential address. A symposium on graduate training in surgery, the afternoon of Dec. 9 will include the following papers:

Background and Current Status of Graduate Surgical Training, Dr. Frank Glenn, New York City.
The Emergency Service in Teaching Hospitals, Drs. John D. Stewart, Harry W. Hale Jr., and Paul A. Kennedy, Buffalo, N. Y.
Residency Training in Private Hospitals, Dr. Guy W. Horsley, Richmond, Va.
Specialty Training with Reference to Gynecology, Dr. Francis B. Carter, Durham, N. C.
The Jacksonville Plan in Post-Graduate Education, Dr. Wilbur C. Sumner, Jacksonville, Fla.

Forty-five papers are scheduled for presentation. Golf tournaments for men and women are planned. At the association dinner, Dec. 10, Dr. Howard A. Patterson, New York City, will serve as toastmaster.

Awards for Rehabilitation Films.—The International Rehabilitation Film Awards will be presented for the third time at the eighth World Congress of the International Society for the Welfare of Cripples in New York City Aug. 28-Sept. 2, 1960. The awards are given "for the best motion picture portraying aspects of services for the physically handicapped which has been released after August 1, 1957, and which is available for showing in 16 mm." To be considered for an award, films must be received in New York City before July 1, 1960. Forty-seven films from 17 different countries were nominated for the International Film Awards at the seventh world congress held in London in 1957. The International Rehabilitation Film Library, operated by the international society, includes 325 prints of 160 different titles. The library operates under the general policies developed by the ISWC's International Film Board. Information concerning the library and the film award can be secured from the International Society for the Welfare of Cripples, 701 First Ave., New York 17.

Meeting on Surgery of the Hand.—The fifth annual meeting of the American Society for Surgery of the Hand will be held Jan. 22-23 at the Palmer House, Chicago. Seventeen papers are scheduled for presentation, the following of which include foreign authors:

Extension of the Distal Phalanx of the Thumb, Dr. R. M. McFarlane, London Ontario, Canada.
An Experimental Study of Digital Flexor Tendon and Healing, Dr. W. K. Lindsay, Toronto, Canada.
Experience with Cross Finger Pedicle Flaps, Dr. J. W. McNichol and Dr. Orville J. Mirehouse, Hamilton, Ontario, Canada.
Tendon Grafting for Division of Flexor Profundus, Dr. Robert Guy Pulvertaft, F.R.C.S., Derby, England.

A discussion on tendon surgery and a question-and-answer period will be conducted by Dr. Pulvertaft, to conclude the meeting. Members of the medical profession are invited. Registration fee is $7; interns and residents will be admitted free. For information and registration, write Dr. George S. Phalen, 2020 E. 93rd St., Cleveland 6, secretary.

New Journal on Experimental Medicine.—*Medicina Experimentalis*, the International Journal of Experimental Medicine, will be published monthly beginning in 1959. It will consist of two volumes of six numbers each per year, and will cost 56 Swiss francs per volume. The journal has four aims: (1) to serve as a link between research workers in other countries, (2) to serve as a link between clinicians, physiologists, and pharmacologists, (3) to present brief communications, not more than four pages, which will contain the essential details of the work involved, (4) to offer new material with a minimum of delay (three months from submission of a manuscript to publication). The journal will publish articles in English, German, and French. The editors are R. Domenjoz, Bonn, Germany; C. H. Best, Toronto, Canada; B. B. Brodie, Bethesda, Md.; J. Cheymol, Paris, France; L. Heilmeyer, Freiburg, Switzerland; and A. Vannotti, Lausanne, Switzerland. The publisher is S. Karger, Basel, Switzerland, and New York City.

Meeting on Industrial Medicine.—The Central States Society of Industrial Medicine and Surgery will hold its winter session in St. Louis Dec. 5 at the Sheraton-Jefferson Hotel. The meeting will be concerned with employment problems in heart diseases, diabetes, gerontology, mental health, and tuberculosis. Specialties and speakers at the morning session, beginning at 10 a. m., are: diabetes, Dr. Joseph T. Beardwood Jr., Philadelphia, chairman, Committee on Employment, American Diabetes Association; gerontology, Dr. William B. Kountz, St. Louis, director of scientific research, Gerontological Research Foundation; mental health, Dr. Addison M. Duval, St. Elizabeth Hospital, Washington, D. C.; and tuberculosis, Mr. Ralph W. Susman director of rehabilitation, National Tuberculosis Association. Dr. Paul Dudley White, Boston, will be guest speaker, presenting "The Relation of Heart Disease to Industry." The afternoon session will be made up of panels which will consist of seven members representing industry, safety, nursing, industrial hygiene, and industrial medicine. For information, write Dr. Allan P. Skoog, 28 E. Jackson Blvd., Chicago 4, secretary-treasurer.

Invite Exhibits for Student Meeting.—Medical students, residents, and interns are invited to prepare scientific exhibits to be displayed at the 10th annual convention of the Student American Medical Association in Los Angeles, May 4-8, 1960. The three exhibits judged most outstanding in both the student and resident-intern categories will win SAMA-Lakeside Awards. The top winners in each category will also have their exhibits featured at the Scientific Exhibit of the American Medical Association during the annual A. M. A. convention in Miami Beach, Fla., in June, 1960. In addition to a prize of $500 and an award certificate, the top winners will receive an expense-free trip to the A. M. A. convention. Second and third prize winners will receive $250 and $100, respectively, and an award citation. Applications for the 1960 SAMA-Lakeside Awards should be sent to the Executive Director, SAMA, 430 N. Michigan Ave., Chicago 11. Deadline for applications is Jan. 1, 1960. Notification of accepted exhibits will be made Feb. 1. Applications should contain the title of the exhibit, a brief description of its physical dimensions, and a 250-300 word report explaining its purpose. Applicants are advised to first check their subject matter with a faculty member or chief.

Medical Exchange Program.—Secretary of Health, Education, and Welfare Arthur S. Flemming announced that the recent visit of Chairman Khrushchev to this country "provided an opportunity for a useful exchange of views on the relationships between representatives of the U. S. Government and of the Soviet Union in the field of health." At a meeting Sept. 26 proposals were discussed for an expansion of the present medical exchange program being carried on by the two nations. In addition to the exchange of delegations such as have been carried on under the Jan. 27, 1959, agreement (Lacy-Zaroubin agreement), it was agreed that the Public Health Service and the U. S. S. R. Ministry of Health will consider the following points with a view to further discussions:

1. Top medical scientists of both nations would exchange visits to study methods of organization of research programs.
2. Exchange of scientific and technical information on an accelerated and systematic basis would be undertaken to identify research trends and accomplishments by scientists and health workers in both nations.
3. Specific research projects would be sought for coordinated studies according to research plans agreed upon by both countries.
4. Exchanges would be initiated between research scientists to work in the laboratories of both countries to familiarize themselves with methods of research and to contribute actively to research projects.

Society News.—Dr. Henry Baker, Boston, was chosen as president-elect of the **American College of Gastroenterology** Sept. 20. Dr. Joseph Shaiken, of Milwaukee, selected president-elect in 1958, assumed the presidency, succeeding Dr. Frank J. Borrelli, of New York City, who became chairman of the board of trustees. Other officers elected were vice-presidents, Drs. Louis Ochs Jr., New Orleans, Edward J. Krol, Chicago, Theodore S. Heineken, Glen Ridge, N. J., and Henry G. Rudner Sr., Memphis, Tenn.; secretary-general, Dr. Lynn A. Ferguson, Grand Rapids, Mich.; secretary, Dr. Louis L. Perkel, Jersey City, N. J.; treasurer, Dr. William C. Jacobson, New York City.——Two staff promotions in the **American Academy of Pediatrics** were announced by Dr. William W. Belford, San Diego, Calif., president of the academy. Dr. Einor H. Christopherson, Evanston, Ill., former executive secretary, was promoted to executive director. Dr. Robert G. Frazier, Evanston, Ill., who was assistant secretary, was promoted to secretary.——The following officers of the **Central Neuropsychiatric Association** were elected at the New Orleans meeting Oct. 16-17: president, Dr. Martin H. Hoffmann, Detroit; president-elect, Dr. Oscar B. Markey, Cleveland; vice-president, Dr. Philip B. Reed, Indianapolis; and secretary-treasurer, Dr. Ralph M. Patterson, Columbus, Ohio. The 1960 meeting will be held at French Lick, Ind., Oct. 14-15.

Dr. Dooley Receives Criss Award.—Dr. Thomas A. Dooley was the recipient of the 1959 Mutual of Omaha Criss Award "for his outstanding contributions to the medically deprived people of the Far East." The award was presented to Dr. Dooley Nov. 10 in Omaha by Dr. Charles W. Mayo, Mayo Clinic, Rochester, Minn., chairman of the Mutual of Omaha Criss Award Board of Judges, and Dr. Jonas E. Salk, Pittsburgh, recipient of the award in 1956 (*immediate past-recipient*). The award was given to Dr. Dooley, Dr. Mayo said, "because of his devotion to the disease-ridden peoples of Laos and Viet Nam. Dr. Dooley's work is truly a remarkable manifestation of a free man helping other free men on a person-to-person basis." Dr. Dooley, with Dr. Peter D. Comanduras, Washington, D. C., founded MEDICO, medical international cooperation organization. At the present time Dr. Dooley is chief of mission for MEDICO in Laos, where his achievements include establishment of two hospitals and a clinic. The Mutual of Omaha Criss Award was created to "encourage and reward outstanding contributions to the health and safety of all peoples." Established to honor Dr. C. C. Criss, founder of the company, who died in 1952, the award consists of $10,000 and a gold medal. Dr. Dooley's address is Box 2, Times Square Station, New York City.

Rehabilitation Fellowship for Japanese Physician.—The creation of an American President Lines' Fellowship for advanced training in physical medicine and rehabilitation for a Japanese physican was announced Nov. 5 simultaneously in Tokyo, San Francisco, and New York. The announcement in Tokyo was made by the Ambassador of the United States of America to Japan, the Hon. Douglas MacArthur II. In San Francisco the announcement was made by Mr. George Killion, president, American President Lines, Ltd., and in New York by Dr. Howard A. Rusk, president, World Rehabilitation Fund. The fellowship, to be given in cooperation with the International Society for the Welfare of Cripples and the Japanese National Committee of the international society, will consist of round-trip travel from Tokyo to New York and a tax exempt stipend of $250 per month or its equivalent. The recipient will be provided with a minimum of one year post-graduate training at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center. The fellowship is the second created by the World Rehabilitation Fund from contributions by the American President Lines. The first fellow was Dr. Enrique Mangalindan, who has completed his fellowship and returned to Manila, where he is on the staff of the National Orthopedic Hospital of the Philippines. Selection of a new recipient will be on the basis of the recommendations of the selection committee established by the Japanese National Committee of the International Society for the Welfare of Cripples. The recipient will begin his training in New York City July 1, 1960, or Jan. 1, 1961.

CORRECTIONS

Saturated and Unsaturated Fat.—In the question and answer on saturated and unsaturated fat, in The Journal, Oct. 24, 1959, page 1164, an error appeared. Emdee contains 28 Gm. of saturated fatty acids per 100 Gm., not 12.7 Gm. Also, the linoleic acid content is 34 Gm. per 100 Gm., not 35.6 Gm.

Doctor-Pilots.—In the article, "The Doctor-Pilots" in The Journal, Oct. 10, page 664, the author's mention of Col. David A. Meyers, an early military flight surgeon, includes a reference to Col. W. C. Eaker. This credit was intended for the late Lieut. Col. William C. Ocker, an Air Corps pilot, who in 1918 demonstrated the practicability of "blind" or instrument flight.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II, Various Cities, April 19-20. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination*. Montgomery, June 21-23. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:[*] On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Colorado:[*] *Examination*. Denver, Dec. 8-9. *Reciprocity*. Denver, Oct. 14. Exec. Sec., Miss Mary M. McConnell, 715 Republic Bldg., 1612 Tremont Place, Denver 2.

Delaware: *Examination*. Dover, Jan. 12-14. *Endorsement*. Dover, Jan. 21. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

District of Columbia:[*] *Examination*. Washington, Dec. 14-15. *Reciprocity*. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Guam: *Subject to Call*. Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Examination*. Honolulu, Jan. 11-12. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination* and *Reciprocity*. Boise, Jan. 11, 12, 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Indiana: *Examination*. Indianapolis, June 1960. *Reciprocity*. Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Iowa:[*] *Examination and Endorsement*. Des Moines, Dec. 7-9. Ex. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines.

Kansas:[*] *Examination and Reciprocity*. Kansas City, Jan. 15-16. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Kentucky: *Examination*. Frankfort, Dec. 14-15. Asst. Sec., Mrs. Ray Wunderlich, 620 South Third St., Louisville 2.

Louisiana: *Examination and Reciprocity*. New Orleans, Dec. 3-5. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

Maryland: *Examination*. Baltimore, Dec. 8-11, Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Massachusetts: *Examination*. Boston, Jan. 12-15. Sec., Dr. David W. Wallwork, Room 37, State House, Boston.

Minnesota:[*] *Examination*. Jackson, June 1960. *Reciprocity*. Jackson, Dec. 7, Sec., Dr. A. L. Gray, Old Capitol, Jackson.

Nebraska:[*] *Examination*. Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

New Jersey: *Examination*. Jan. 19-22. *Reciprocity*. Monthly, Admin. Sec., Michael E. H. Sweeney, 28 West State St., Trenton.

New York: *Examination*. Albany, Buffalo, New York and Syracuse, Dec. 8-11. Sec., Dr. Stiles D. Ezell, 23 South Pearl St., Albany.

North Dakota: *Examination*. Grand Forks, Jan. 6-8. *Reciprocity*. Grand Forks, Jan. 9. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

Ohio: *Examination*. Columbus, Dec. 15-17. *Endorsement*. Columbus, Oct. 5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

Oregon:[*] *Examination and Reciprocity*. Portland, Jan. 13-16. Ex. Sec., Mr. Howard J. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination*. Philadelphia, January. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

South Carolina: *Examination and Endorsement*. Columbia, Dec. 8-9. Sec., Dr. H. E. Jervey, Jr., 1329 Blanding St., Columbia.

Texas:[*] *Examination*. Fort Worth, Dec. 3-5. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination*. Salt Lake City, July 6-8. *Reciprocity*. Salt Lake City, Nov. 17. Director, Mr. Frank E. Lees, 324 State Office Bldg., Salt Lake City 1.

Virginia: *Reciprocity*. Dec. 1, *Examinations* Dec. 2-4 inclusive, Richmond. Address: Board of Medical Examiners, 631 First St. S. W., Roanoke.

Washington:[*] *Examination*. Seattle, Jan. 11-13. Administrator, Professional Division, Capitol Bldg., Olympia.

West Virginia: *Examination*. Charleston, Jan. 11-13. Sec., Dr. Newman H. Dyer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:[*] *Examination*. Madison, Jan. 14-16. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Building, 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity*. Cheyenne, Feb. 1. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

South Dakota: *Examination*. Vermillion, Dec. 4-5. Dr. Gregg M. Evans, 310 East 15th St., Yankton.

Washington: *Examination*. Seattle, Jan. 6-7. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

Wisconsin: *Examination*. Milwaukee, Dec. 5, Madison, Apr. 9, Sec., Mr. Wm. H. Barber, 621 Ranson St., Ripon.

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[*] Basic Science Certificate required.

DEATHS

Allison, Charles Newton, San Diego, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; died in the Mercy Hospital Sept. 5, aged 78.

Anderson, John Percy Ⓜ Cleveland; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1920; specialist certified by the American Board of Internal Medicine; member of the American College of Chest Physicians; fellow of the American College of Physicians; served on the faculty of Western Reserve University School of Medicine; chief of medicine at the Euclid-Glenville Hospital in Euclid; senior medical consultant, St. Vincent Charity Hospital; died in the Cleveland Clinic Hospital Sept. 5, aged 62.

Barnes, Earl Bower Ⓜ Washington, D. C.; born in San Antonio, Texas, July 8, 1913; University of Texas School of Medicine, Galveston, 1939; interned at the Gallinger Municipal Hospital, where he served a residency; associate professor of surgery at the Georgetown University School of Medicine; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; veteran of World War II; consultant, Veterans Administration Hospital; associated with the Prince George's General Hospital in Cheverly, Md., District of Columbia General Hospital, and Georgetown University Hospital, where he died Sept. 12, aged 46.

Beckett, Austin L., Lexington, Ky.; Hospital College of Medicine, Louisville, 1907; retired clinical director at the Eastern State Hospital; died Sept. 10, aged 76.

Bensel, Walter, New York City; Columbia University College of Physicians and Surgeons, New York City, 1890; veteran of World War I; a founder of the New York Cardiological Society, and was president from 1940 to 1949, when he became chairman of the board; for many years sanitary superintendent of the New York City Health Department; associated with the Manhattan General and New York hospitals; died in Oxford, Md., Sept. 16, aged 90.

Bergenstal, Delbert Mauritz Ⓜ Medical Director, U. S. Public Health Service, Bethesda, Md.; born in Kansas City, Mo., Dec. 23, 1917; University of Chicago, The School of Medicine, 1947; received a Ph.D. from Purdue University in Lafayette, Ind., in 1944; certified by the National Board of Medical Examiners; member of the American Rheumatism Association, Central Society for Clinical Research, the American Society for Clinical Investigation; American Federation for Clinical Research, Endocrine Society, Phi Beta Kappa, Alpha Omega Alpha, and Sigma Xi; member Endocrinology Panel of Cancer Chemotherapy, National Service Center; interned at the Presbyterian Hospital in New York City, where he served a residency; served a residency at the University of Chicago Clinics; formerly on the faculty of his alma mater and full-time director of section on arthritis and rheumatic diseases (was on leave from University position at time of his death); veteran of World War II; in 1956 joined the National Cancer Institute, where he was assistant chief of endocrinology; died in the Clinical Center of the National Institutes of Health Sept. 12, aged 41.

Bracey, Altamont Hart Ⓜ South Hill, Va.; Medical College of Virginia, Richmond, 1928; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; member of the South Hill Chamber of Commerce; formerly on the staff of the Stevens Clinic Hospital in Welch, W. Va., where for seventeen years he was head of the department of traumatic surgery; associated with the Community Memorial Hospital, where from 1954 to 1956 he was first chief of staff, and where he died Sept. 11, aged 58.

Breslin, John George Ⓜ Boston; Harvard Medical School, Boston, 1911; fellow of the American College of Surgeons; served on the faculty of Tufts College Medical School; retired as chief of surgery with the out-patient department of the regional office of the Veterans Administration; died Sept. 13, aged 72.

Brooks, John Eugene, Eastport, Maine; McGill University Faculty of Medicine, Montreal, Que., Canada, 1903; for many years served as chairman of the school board of Eastport; veteran of World War I; for many years associated with the U. S. Public Health Service; died Sept. 9, aged 85.

Brown, Gerster William Ⓜ Oklahoma City, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1930; member of the Industrial Medical Association; veteran of World War II; associated with the Mercy, Polyclinic, and Wesley hospitals; died in Eagle, Colo., Sept. 2, aged 56.

Browne, Paul Zollicoffer Ⓜ Lakeland, Colo.; Tulane University School of Medicine, New Orleans, 1915; veteran of World Wars I and II; associated with the U. S. Veterans Administration in Denver; died Sept. 6, aged 70.

Ⓜ Indicates Member of the American Medical Association.

Burnell, Max Ronald Ⓜ Flint, Mich.; born in Metamora, Mich., Oct. 6, 1893; University of Michigan Medical School, Ann Arbor, 1918; retired medical director of the General Motors Corporation, where he organized the medical department of the AC Spark Plug Division in 1931; presented the William S. Knudsen award for outstanding contributions to industrial medicine; received a meritorious service award of the American Cancer Society; instructor at the Long Island College Hospital in Brooklyn from 1918 to 1921; advisor at the University of Michigan Social Science Research Project; medical advisor, National Association of Manufacturers; for many years medical advisor at the Clara Elizabeth Fund; from 1950 to 1952 member of the board of governors of the University of Michigan Institute of Industrial Health; served as chairman of the Michigan Industrial Health Commission; fellow of the American College of Surgeons; member of the American Academy of Occupational Medicine and the Industrial Medical Association; member of the Sigma Chi and Nu Sigma Nu; chief of staff, Women's Hospital from 1945 to 1948; associated with the Hurley Hospital and the McLaren General Hospital, where he died Sept. 19, aged 65.

Burnight, Ernest Robert, Pismo Beach, Calif.; Rush Medical College, Chicago, 1925; formerly associated with the U. S. Public Health Service; veteran of World Wars I and II; died in the French Hospital, San Luis Obispo, Sept. 4, aged 67.

Cantril, Simeon Theodore Ⓜ Seattle; born in Hyrum, Utah, Feb. 17, 1908; Harvard Medical School, Boston, 1932; interned at the Michael Reese Hospital in Chicago, where he served a residency; certified by the National Board of Medical Examiners; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; in 1957 was presented with the Janeway medal of the American Radium Society, of which he was a member; each year the medal is presented to a physician or scientist who made important contributions to radiation treatment in the field of medicine; also gave the Janeway Lecture; at one time on the staff of the Curie Foundation in Paris, France; during World War II was drafted to take part in the Manhattan atomic project and was at the University of Chicago when nuclear fission first was accomplished there; formerly medical director of the Oak Ridge atomic plant in Tennessee; later, assistant medical director at the Hanford (Wash.) Plutonium Works; chairman of the advisory committee on biology and medicine of the Atomic Energy Commission; author of two books; since 1938 director of the Tumor Institute of the Swedish Hospital, where he died Sept. 10, aged 51.

Carnes, Moses Ⓜ Forest Hills, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1921; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; served as diagnostician for the department of health in New York City; associated with the Jewish Hospital and Kingston Avenue Hospital, Brooklyn, and the Long Island Jewish Hospital in New Hyde Park; died Sept. 7, aged 63.

Chapman, Kenneth William Ⓜ Medical Director, U. S. Public Health Service, Bethesda, Md.; born in Springfield, Mass., Jan. 6, 1911; Yale University School of Medicine, New Haven, 1938; interned at the U. S. Marine Hospital in Stapleton, Staten Island, N. Y.; joined the U. S. Public Health Service in 1939; assistant chief of the Public Health Service Division of Hospitals in Washington, D. C., from 1950 to 1952 when he became chief of the Public Health Service Narcotics Hospital in Lexington, Ky., serving until 1954; served with the National Institute of Mental Health as consultant to state and community hospitals and health agencies on the medical problems of narcotic addiction; since 1957 associate director of the Clinical Center, National Institutes of Health, where he supervised the patient care departments of this combined and laboratory research facility; specialist certified by the American Board of Psychiatry; fellow of the American College of Physicians and the American Psychiatric Association; died Sept. 18, aged 48.

Cinquegrana, Margaret, North Seekonk, Mass.; Middlesex University School of Medicine, Waltham, Mass., 1936; died in Our Lady of Fatima Hospital, Providence, R. I., Sept. 7, aged 55.

Cochrane, Charles Stites Ⓜ Brooklyn; Long Island College Hospital, Brooklyn, 1900; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; associated with the Kings County, Samaritan, Brooklyn State, and Carson C. Peck Memorial hospitals; died in the Maimonides Hospital Sept. 5, aged 80.

Coffey, Stanley Edward Ⓜ Imola, Calif.; University of California School of Medicine, San Francisco, 1927; veteran of World War I; member of the staff of the Napa State Hospital; died in Queen of the Valley Hospital in Napa Sept. 16, aged 62.

Colucci, John Anthony Ⓜ New York City; Cornell University Medical College, New York City, 1916; died Sept. 16, aged 68.

Comfort, Milton Douglas Ⓜ Flat Rock, Mich.; University of Western Ontario Faculty of Medicine, London, Ont., Canada, 1928; member of the American Academy of General Practice; interned at the

Harper Hospital in Detroit; on the staff of the Mercy Hospital in Monroe; died in the Wyandotte (Mich.) Hospital Sept. 8, aged 54.

Corrado, John Charles, Boston; Middlesex University School of Medicine, Waltham, Mass., 1932; interned at the Hospital of the Holy Family in Brooklyn; died in the Chelsea Memorial Hospital in Chelsea, Mass., Sept. 14, aged 50.

Cox, Lloyd H. Ⓜ Dayton, Ohio; Howard University College of Medicine, Washington, D. C., 1904; for many years active on the All-Dayton committee and the home service committee of the Montgomery County chapter of the American Red Cross; served as chairman of the board of directors of the YMCA; died Sept. 8, aged 79.

Craig, Will Newton, Stanford, Ky.; Louisville (Ky.) Medical College, 1895; also a pharmacist; first president of the Lincoln County Historical Society, of which he was a charter member; past-president of the Rotary Club; died Sept. 10, aged 88.

Delavau, Joseph Rasbold, Wynnewood, Pa.; Medico-Chirurgical College of Philadelphia, 1905; died June 5, aged 77.

Donohue, William Edward Ⓜ Manitowoc, Wis.; Northwestern University School of Medicine, Chicago, 1910; fellow of the American College of Surgeons; past-president and treasurer of the Manitowoc County Medical Society; served overseas during World War I; associated with the Two Rivers (Wis.) Municipal Hospital, Memorial Hospital in Manitowoc, and the Holy Family Hospital, where he was staff president and treasurer, and where he died Sept. 6, aged 76.

Fein, Bernard Samuel Ⓜ Newark, N. J.; Cornell University Medical College, New York City, 1924; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; veteran of World War I; on the staffs of the Babies' Hospital-Coit Memorial and the Newark Beth Israel Hospital; died Sept. 11, aged 59.

Feldman, William, Stephens, Ark.; St. Louis College of Physicians and Surgeons, 1918; Kansas City (Mo.) College of Medicine and Surgery, 1923; died Sept. 11, aged 73.

Feuerstein, Samuel S., Long Island City, N. Y.; University and Bellevue Hospital Medical College, New York City, 1925; member of the American College of Gastroenterology; a founder of the Queens County Society of Internal Medicine; served on the staffs of the Triboro Hospital of Queens Hospital Center, where he was director of gastroenterology and associate in medicine, Queens General Hospital in Jamaica; founder and director of the Boulevard Hospital, where he died Sept. 3, aged 58.

Fisher, Arthur Lawrence Ⓜ San Carlos, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1900; veteran of World War I; fellow of the American College of Surgeons; for many years practiced in San Francisco, where he served on the staffs of Mount Zion and Stanford University hospitals; died in the Stanford University Hospital in San Francisco, Sept. 10, aged 83.

Fisher, Cornelius J., Holland, Mich., Detroit College of Medicine, 1894; served on the board of the Holland City Hospital; died Sept. 11, aged 93.

Fletcher, Emanuel Ⓜ Flushing, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1927; specialist certified by the American Board of Pediatrics, Inc.; member of the American Academy of Pediatrics; associated with the Flower and Fifth Avenue Hospitals in New York City, Flushing (N. Y.) Hospital, and the Queens General Hospital in Jamaica; died in the Flushing Hospital Sept. 5, aged 55.

Foster, John Ⓜ New Castle, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1894; fellow of the American College of Surgeons; past-president of the Lawrence County Medical Society; served as chief of surgical staff at Jameson Hospital and New Castle Hospital; died Aug. 25, aged 86.

Franklin, Floyd Shock Ⓜ Dallas, Texas; Baylor University College of Medicine, Dallas, 1931; associated with the Methodist, Gaston, St. Paul, and Baylor University hospitals; died Sept. 9, aged 54.

Ginn, Curtiss, Dayton, Ohio; Cleveland University of Medicine and Surgery, 1895; fellow of the American College of Surgeons; served on the medical staffs of Miami Valley, St. Elizabeth, and Dayton State hospitals; for many years surgeon for the Dayton Power & Light Company; died Sept. 10, aged 87.

Gottsch, John Erwin Ⓜ Tampa, Fla.; born in Shenandoah, Iowa, Sept. 23, 1923; State University of Iowa College of Medicine, Iowa City, 1947; interned at the Charity Hospital of Louisiana in New Orleans, where he served a residency; certified by the National Board of Medical Examiners; specialist certified by the American Board of Orthopaedic Surgery; fellow of the American College of Surgeons; member of the American Academy of Orthopedic Surgeons; served as chief orthopedic surgeon and orthopedic consultant at the U. S. Air Force Hospital, MacDill Air Field Base; associated with the Clara Frye Tampa Negro Hospital, St. Joseph's Hospital, and Tampa Municipal Hospital; died Sept. 9, aged 35.

Griffin, Frank Joseph, River Forest, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908; served as neuropsychiatrist for the U. S. Veterans Bureau;

formerly superintendent of the Chicago State Hospital; died in Oak Park (Ill.) State Hospital Sept. 14, aged 80.

Haight, Thomas Hulen Ⓜ New York City; Harvard Medical School, Boston, 1948; interned at the Boston City Hospital, where he served a residency; at one time teaching fellow in medicine at his alma mater; certified by the National Board of Medical Examiners; assistant professor of medicine, preventive medicine, and public health, and consultant assistant professor of pediatrics, University of Oklahoma School of Medicine and University Hospitals in Oklahoma City; served in the U. S. Naval Reserve from Oct. 1, 1952, to Oct. 3, 1954; died Sept. 3, aged 33.

Hanser, Otto C. Ⓜ St. Louis; St. Louis College of Physicians and Surgeons, 1918; member of the American Academy of Medicine; on the staff of the Lutheran Hospital, where he died Sept. 14, aged 76.

Harding, Lewis William, Lexington, Ky.; State University of Iowa College of Medicine, Iowa City, 1890; for many years on the faculty of his alma mater, where he organized the department of anesthesiology; taught anesthesiology at the College of Medical Evangelists at Loma Linda and Los Angeles; died Sept. 1, aged 93.

Harkness, Carleton Ainslie Ⓜ Owosso, Mich.; Chicago Homeopathic Medical College, 1904; the Hahneman Medical College and Hospital, Chicago, 1905; fellow of the American College of Surgeons; veteran of World War I; staff member at the Memorial Hospital, where he died Aug. 19, aged 78.

Hearst, Allen Lorin Ⓜ Kansas City, Mo.; Ensworth Medical College, St. Joseph, 1897; veteran of World War I; asociated with the Trinity Lutheran Hospital; died Sept. 9, aged 83.

Henry, Leonard Lester Ⓜ Lansing, Mich.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1923; member of the Industrial Medical Association; died Aug. 25, aged 59.

Herrmann, Edgar Thomas Ⓜ St. Paul, Minn.; University of Minnesota Medical School, Minneapolis, 1919; fellow of the American College of Physicians; clinical assistant professor of internal medicine at his alma mater; died in the Charles T. Miller Hospital Aug. 26, aged 66.

Hicks, Arthur, Scott, Ark. (licensed in Arkansas in 1904); died Sept. 2, aged 78.

Holcomb, Norman Franklin Ⓜ Marshall, Texas; Tulane University School of Medicine, New Orleans, 1940; interned at the Southern Baptist Hospital in New Orleans; served a residency at the Texas and Pacific Railway Employees Hospital in Marshall; associated with the Memorial Hospital; died Aug. 26, aged 48.

Hopper, Edward Bernard Ⓜ Captain, M.C., U. S. Navy, Purchase, N. Y.; born in Purchase, Feb. 8, 1906; Yale University School of Medicine, New Haven, Conn., 1929; appointed first lieutenant in the Army of the United States on April 22, 1936, and a lieutenant commander in the U. S. Naval Reserve on April 22, 1943; reported for active duty June 14, 1943; commissioned a commander in the regular U. S. Navy Aug. 14, 1946; assigned to U. S. Naval Supply Center in Oakland, Calif.; specialist certified by the American Board of Obstetrics and Gynecology; at one time on the staffs of the Stamford (Conn.) Hospital and St. Joseph's Hospital in Stamford, Conn.; died in Vallejo, Calif., June 30, aged 53.

Hornsby, William Boyd, Clinton, Mich.; University of Louisville (Ky.) Medical Department, 1911; for many years associated with the Herrick Hospital in Tecumseh; died in Mercy Hospital, Grayling, Sept. 9, aged 74.

Howell, Orion Emmet Ⓜ Norman, Okla.; Central Medical College of St. Joseph, Mo., 1900; associated with the Norman Municipal Hospital; died Sept. 13, aged 82.

Johnson, Clarence Arthur Ⓜ Los Angeles; Rush Medical College, Chicago, 1910; fellow of the American College of Surgeons; veteran of World War I; emeritus consulting surgeon to the Methodist Hospital, Hollywood Presbyterian Hospital and the Crenshaw Hospital; died Aug. 27, aged 78.

Kilgore, Byron, Indianapolis; Medical College of Indiana, Indianapolis, 1905; veteran of World War I; at one time served as physician at Shortridge High School; died in the Robert W. Long Hospital Aug. 29, aged 77.

Lund, Frederic Albert, New London, Conn.; New York Homeopathic Medical College and Hospital, New York City, 1900; served on the faculty of his alma mater; died Sept. 22, aged 85.

McDermott, Neil Thomas Ⓜ Cleveland; Harvard Medical School, Boston, 1932; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychiatric Association; served on the faculty of Western Reserve University School of Medicine; formerly medical director of the Ingleside Hospital; consultant to Benjamin Rose Hospital and on the staffs at University and St. Alexis hospitals; died Aug. 24, aged 54.

McGahey, Robert Goodloe, Birmingham, Ala.; Birmingham Medical College, 1912; associated with the Birmingham Baptist Hospital; died in St. Vincent's Hospital Aug. 21, aged 72.

Manley, John Edward Ⓜ Scranton, Pa.; Jefferson Medical College of Philadelphia, 1928; twice elected president of the Lackawanna County Heart

Association, of which he was one of the founders; served as president of the Lackawanna County Medical Society; veteran of World War II; chief of medicine at the Scranton State Hospital; cardiologist at Mercy and St. Mary's hospitals; died in the Jefferson Hospital, Philadelphia, Sept. 3, aged 54.

Mart, John Arthur Ⓜ Chicago; Northwestern University Medical School, Chicago, 1938; interned at the Wesley Memorial Hospital in Chicago; served a residency at the Healthwin Hospital in South Bend, Ind., and the Passavant Memorial Hospital, where he served a fellowship in internal medicine; an associate in medicine at his alma mater; served on the staff of the Passavant Memorial Hospital; at one time medical counselor for the *Chicago Tribune;* died Sept. 12, aged 50.

Martzowka, Martin Andrew Ⓜ Roscommon, Mich.; University of Michigan Medical School, Ann Arbor, 1931; member of the Gerrish-Higgins High School Board of Education for 12 years and board president at the time of his death; a charter member and past-president of Rotary Club of Roscommon; on the staff of the Mercy Hospital in Grayling, where he died Sept. 7, aged 55.

Mearns, Jack Greene Ⓜ Manhattan Beach, Calif.; University of Illinois College of Medicine, Chicago, 1931; association with the U. S. Public Health Service terminated Sept. 4, 1943; on the staff of the Jared Sidney Torrance Memorial Hospital in Torrance; died in Palo Alto Aug. 27, aged 57.

Mercer, John Lantry Ⓜ Rochester, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1934; past-president of the Rochester Academy of Medicine; clinical instructor in medicine at the University of Rochester School of Medicine and Dentistry; on the staffs of the Highland and Strong Memorial hospitals; associated with the Genessee Hospital, where he served an internship and residency, and where he died Aug. 30, aged 51.

Mills, Errold Victor, Vinalhaven, Maine; Middlesex College of Medicine and Surgery, Cambridge, Mass., 1922; died Aug. 31, aged 76.

Monaco, Attilio Ⓜ Elmhurst, Ill.; Bennett Medical College, Chicago, 1914; died in the Michael Reese Hospital Sept. 20, aged 82.

Morrison, Robert Raymond Ⓜ Dunbar, Pa.; Jefferson Medical College of Philadelphia, 1919; served on the staff of the Connellsville (Pa.) State Hospital; died Aug. 24, aged 64.

Myers, Rienzi Verne Ⓜ Mansfield, Ohio; Western Reserve University Medical Department, Cleveland, 1909; served on the advisory board of the U. S. Draft Boards during World Wars I and II; associated with the Mansfield General Hospital; past-president of the Richland County Medical Society; died in the Madison Hospital Aug. 20, aged 78.

Owens, Alexander Charles Kingsley, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1897; died in the Suburban General Hospital, Bellevue, Pa., June 6, aged 89.

Paris, Arthur Sterling Ⓜ Balboa, Calif.; University of Nebraska College of Medicine, Omaha, 1943; interned at the Swedish Hospital in Seattle; served a residency at the Ball Memorial Hospital in Muncie, Ind., and the Orange County General Hospital in Orange; veteran of World War II; on the staff of Hoag Memorial Hospital, Newport Beach; died in Pacific Ocean Aug. 16, aged 41.

Rauch, Elias Ⓜ New York City; Long Island College Hospital, Brooklyn, 1924; *specialist certified* by the American Board of Obstetrics and Gynecology; associated with St. Joseph Hospital, Far Rockaway, and New York Polyclinic Medical School and Hospital and the Harlem Hospital; died in the Lenox Hill Hospital Aug. 25, aged 58.

Replogle, Henry Brown, Altoona, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1906; associated with the Mercy Hospital; died Aug. 18, aged 77.

Robb, James Bryson Ⓜ College Park, Md.; Rush Medical College, Chicago, 1903; served in Lucas County, Iowa, as county coroner, county physician, and member of the Lucas County Insane Commission; formerly practiced in Chariton, Iowa; surgeon for the Burlington Railroad; died in the George Washington University Hospital, Washington, D. C., Sept. 5, aged 83.

Sarfatty, Isaac Joshua Ⓜ Milwaukee; Marquette University School of Medicine, Milwaukee, 1934; specialist certified by the American Board of Psychiatry and Neurology; fellow of the American Psychiatric Association; on the faculty of Marquette University School of Medicine; past-vice-president of the Milwaukee County Mental Health Association and past-president of the Milwaukee County Neuropsychiatric Society; veteran of World War II; formerly connected with the Veterans Administration in Madison; served as chief of psychiatric services at the Veterans Administration regional office; on the staff of the Milwaukee Sanitarium; died at the Mayo Clinic, Rochester, Minn., Aug. 30, aged 57.

Scholpp, Otto Wendell Ⓜ Hutchinson, Minn.; Baltimore Medical College, 1907; specialist certified by the American Board of Radiology, Inc.; member of the Radiology Society of North America and the American College of Radiology; on the staff of the Hutchinson Community Hospital; died Aug. 26, aged 80.

Sherman, Elbert Stetson Ⓜ Newark, N. J.; born in Manasquan, N. J., Aug. 5, 1873; University of Pennsylvania Department of Medicine, Philadelphia, 1897; veteran of World War I; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; served as a member of the board of managers of the New Jersey Commission for the Blind, of which he was secretary, as chairman of the State Society Advisory Committee for the Conservation of Vision, and as a member of the New Jersey Procurement and Assignment Service; associated with the Newark Eye and Ear Infirmary, Presbyterian, and Babies' Hospital in Newark; consultant at Monmouth Memorial Hospital in Long Branch, and the Fitkin Memorial Hospital in Neptune; died Sept. 11, aged 86.

Shick, Simon Loeb Ⓜ Jamaica, N. Y.; Long Island College of Medicine, Brooklyn, 1930; specialist certified by the American Board of Obstetrics and Gynecology; veteran of World War II; associated with the Kew Gardens (N. Y.) Hospital, Queens General Hospital, and Jamaica Hospital, where he served an internship, and where he died Aug. 18, aged 54.

Siegel, Jacob Ross Ⓜ Philadelphia; Temple University School of Medicine, Philadelphia, 1934; interned at the Wesley Hospital and Sedgwick County Hospital in Wichita, Kan.; formerly associated with the Indian Service; veteran of World War II; died in the southern division of the Albert Einstein Medical Center, Sept. 10, aged 49.

Simpson, Lora Alonzo, Mount Ida, Ark. (licensed in Arkansas in 1903); died in St. Joseph's Hospital, Hot Springs, Aug. 23, aged 84.

Stadie, William Christopher, Philadelphia; born in New York City June 5, 1886; Columbia University College of Physicians and Surgeons, New York City, 1916; member of the American Society for Clinical Investigation, Harvey Society, National Academy of Sciences, American Philosophical Society, and the American Society of Biological Chemists, of which he was treasurer from 1941 to 1945; received the John Phillips Memorial Medal of the American College of Physicians for 1941; in July, 1955, at the annual meeting of the Association of American Physicians received the Kober Medal, awarded annually by the Kober Foundation at Georgetown University, Washington, D. C., to a member of the association; in 1956 received the Banting Medal of the American Diabetes Association; member of the College of Physicians of Philadelphia, which on July 14, 1957, awarded him the Alvarenga Prize; since 1956, emeritus professor of research medicine at the University of Pennsylvania School of Medicine, where he joined the faculty in 1925 as associate professor of research medicine, serving in this capacity until 1941 when he became John Herr Musser professor of research medicine; at one time assistant professor of medicine, Yale University School of Medicine, New Haven, Conn.; veteran of World War I; in 1944, served with the Office of Scientific Research and Development of the U. S. Public Health Service; consultant to the division of metabolic diseases, National Institutes of Health; from 1918 to 1921 an assistant and associate at the Hospital of the Rockefeller Institute in New York City; from 1942 to 1947, member of the editorial board of the *Journal of Biological Chemistry;* editor of *Diabetes;* died in Middletown, N. Y., Sept. 11, aged 73.

Starbird, Edward Perley Ⓜ Boston; Harvard Medical School, Boston, 1894; veteran of the Spanish-American War; for many years served as consultant and trustee at Chelsea Soldiers Home; affiliated with the McLean Hospital, Waverley, Boston City Hospital, Boston Lying-in Hospital, House of the Good Samaritan, and St. Margaret's Hospital; died Aug. 25, aged 87.

Stewart, William Cyrus Ⓜ Kenosha, Wis.; St. Louis University School of Medicine, 1912; past-president of the Kenosha County Medical Society; associated with Kenosha and St. Catherine's hospitals; died Aug. 23, aged 74.

Stiles, Frank Jr. Ⓜ East Lansing, Mich.; University of Michigan Medical School, Ann Arbor, 1930; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; past-president of the Detroit Dermatological Society; veteran of World War II; associated with Edward W. Sparrow and St. Lawrence hospitals; died Aug. 23, aged 57.

Valenta, Henry James Ⓜ Reno, Nev.; Loyola University School of Medicine, Chicago, 1935; veteran of World War II; on the staff of St. Mary's Hospital; died Aug. 30, aged 48.

Watterson, Robert Wayne, Darlington, Pa.; Jefferson Medical College of Philadelphia, 1916; served on the staff of the Providence Hospital in Beaver Falls; died in the Allegheny General Hospital, Pittsburgh, Aug. 23, aged 68.

Wilkinson, John Norman Ⓜ Seattle; University of Virginia Department of Medicine, Charlottesville, 1928; interned and trustee at the Virginia Mason Hospital, where he died Aug. 28, aged 54.

Wronker, Simon Lewis Ⓜ Fort Lauderdale, Fla.; Long Island College Hospital, Brooklyn, 1916; member of the American Academy of General Practice; veteran of World War I; formerly practiced in Rochester, N. Y., where he was associated with the Highland Hospital; died Sept. 1, aged 69.

FOREIGN LETTERS

FRANCE

Fractioning Body Weight.—L. Justin-Besançon and co-workers (*Presse méd.* 67:1415, 1959), studied emaciation and obesity from the standpoint of plasma, extracellular liquid, and total water volumes. The extracellular fluid volume was determined in 34 emaciated persons. It remained close to the physiological 15% of the total body weight if based on the subjects ideal weight. Inflation of the extracellular fluid volume gives rise to an increase of total sodium. In the normal subject water accounts for 58%, lipids for 20%, and solids for 22% of the total body weight. These values were compared with the results obtained in emaciated subjects. As an average, in the latter, the proportion of total water was increased, that of extracellular water was around the normal value, and that of lipids was low (9.9% in men and 15.7% in women). Repeated determinations were of value in following tissular recovery in convalescent patients and the results of dietary treatment. True obesity may be defined as any state in which the proportion of lipids exceeds 30% of the body weight.

Kernicterus.—M. Lacomme and co-workers (*Presse méd.* 67:1383, 1959), confirmed that when maintaining the bilirubin blood level below 18 to 20 mg. per 100 ml. with exchange transfusions the danger of kernicterus tends to disappear during the course of a hemolytic disease in a neonate. Nevertheless, the problem of kernicterus is not entirely solved and, as the clinical data that allow its diagnosis are not precise, it is difficult to evaluate its frequency and therefore to compare statistical studies. The authors state that hyperextension of the neck and athetosic movements are pathognomonic if both are present on the first days of life. A three-year follow-up study of 94 patients with hemolytic disease from anti-Rh isoimmunization seen in 1955 and 1956 indicated that apart from the classic forms (with the typical neonatal syndrome and the remission in the second month) a partially or totally regressive form is becoming common.

Tuberculous Lesions in Excised Lungs.—F. Franchel and co-workers (*Presse méd.* 67:1302, 1959) have modified their previous conceptions of the pathology of pulmonary tuberculosis as a result of the study of 117 excised lungs. Of the 117 patients, 42 were operated on after poor medical treatment. Of these 42 patients, 13 had histological findings that were frankly evolutive. Of 75 patients who had been adequately treated 17 had frankly evolutive histological findings. There was a close correlation between histological appearance and results of bacteriological examination. A detailed study of nonprogressive cases with negative results of bacteriological examination showed that most of these patients had received the three principal antibiotics for an average of 13 months. For the most part, medical failures were due to a poor technique of antibiotic treatment. Of the 117 lung excisions 100 were manifestly justified by the histological and bacteriological findings. Only two seemed completely cured and 15 had a stationary appearance, which made the utility of the operation questionable.

Complications of Typhoid.—J. Thiodet and co-workers (*Presse méd.* 67:1305, 1959) stated that the biochemical and electrocardiographic study of more than 100 patients with typhoid showed the importance of biochemical factors in the genesis of the cardiovascular manifestations of the disease. Potassium plays an important part and the various electrocardiographic aspects that have been described in typhoid fever are indicative of metabolic disorders. Protein catabolism, fasting, dehydration, and fever are the chief factors causing potassium imbalance in patients with typhoid. The cellular atony resulting from this imbalance, sometimes aggravated by inadequate therapy, is responsible for the major associated cardiovascular accidents.

Hyperoxalemia in Gout.—A. Mugler (*Presse méd.* 67:1309, 1959) showed that in gout, in addition to typical metabolic symptoms characterized by hyperuricemia, there are other metabolic complications due to hyperoxalemia. He found an increased oxalic acid level in 80% of all patients with hyperuricemia and when only patients with gout were considered he found hyperoxalemia in 85%. The urine sediment of gouty patients often contains oxalic acid crystals. The author concluded that an oxalic rheumatism probably exists. This may explain attacks of gout in patients with a normal uric acid level.

Idiopathic Pneumothorax.—Georges Thomeret (*Presse méd.* 67:1353, 1959) studied a series of 11 patients who had idiopathic pneumothorax. Roentgenography, pleuroscopy, and exploratory operations showed that idiopathic pneumothorax was caused by the bursting of pulmonary "bubbles."

The items in these letters are contributed by regular correspondents in the various foreign countries.

Microscopic sections of this region showed an atrophy of the walls of the alveoli, often associated with chronic inflammation. This type of localized emphysema is to be distinguished from diffuse or regional emphysema.

Its cause is unknown, but the clinical findings of idiopathic pneumothorax are sufficiently characteristic to form a clinical entity. Idiopathic pneumothorax is exclusively a disease of the young adult, especially young men, who appear in perfect health. Sometimes a respiratory effort seems to be the direct cause, but in most patients no cause is recognized. The onset of the disease is characterized by pain and dyspnea, which are extremely variable and expose the diagnosis to numerous errors. The diagnosis is confirmed by roentgenograms, which may show pleural adhesions on the collapsed side and, in rare cases, "bubbles" on the opposite side. Idiopathic pneumothorax may be complicated by (1) an increase in pressure leading to bilateral pneumothorax which may result in death from asphyxia and (2) hemopneumothorax, a late complication, in which bleeding follows a rupture of an adhesion and is generally massive. The disease may become chronic with development of a thick pleurovisceral membrane encircling the lung, or the patient may be cured, in which case his susceptibility to ipsilateral or contralateral recurrence is much greater than average.

Memory Elements in Computers.—At the first International Conference on Information Processing sponsored by UNESCO in Paris in June, D. G. Willis reported that human beings were perhaps the only examples of truly effective learning and pattern recognition automata. We can estimate that the human memory capacity lies with good probability in the range of 10^{10} to 10^{16} units of information. At the same time, the number of neurons in a human system is close to 10^{10}. If we make the assumption that human memory is associated with neurons we may say that on the average one neuron can store between 1 and 1 million units of information. Much has been done in the analysis of formal neuron systems whose elements do not change their logical properties with their activity. Since such neurons can store at most one unit of information each, they probably cannot provide an adequate model for human memory. Neurophysiologists have long envisioned the possibility of plastic neurons or neurons which change their logical properties with their activity.

Although it has not yet been possible to observe such behavior in human neurons, several models of this kind have been suggested, such as those of Eccles, Hebb, and Shimbel. After studying a neuron model the speaker found that it was possible to read information into and out of single neurons of this kind simply by adopting an artifice of two separate read-in leads with absolute excitatory and inhibitory capacity. The read-in and read-out properties of a system of 288 plastic neurons were simulated on a digital computer and an expression was derived for the output of a plastic neuron as a function of its previous history. The necessity for the artifice of absolute excitation and inhibition may be removed by considering a large system of neurons containing feedback connections. In conclusion it was proved that this kind of plastic neuron model was compatible with the large capacity and with the apparent random access character of human memory.

Survival with Hodgkin's Disease.—At a meeting of the National Academy of Medicine in March Dr. G. Marchal reported a series of 150 patients with Hodgkin's disease. Of these, 48 died in the first year of intestinal perforation or occlusion, mediastinal or abdominal adenopathies, pulmonary involvements, or paraplegia; 30 patients died in the second year of similar complications; 20 died in the third year, 16 in the fourth, and 10 in the next year. The expectation of survival for the patients who receive regular and early treatment varies between three and seven years. Survival beyond the eighth year is rare, although the author observed one 14-year survival. The prognosis is established not only by the localization of the disease and the number and type of complications but also by the sedimentation rate and increase of alpha-2 globulins and of haptoglobulins rather than increase of fibrinogen.

Deaths from Tuberculosis.—At the same meeting, Dr. E. Bernard reported that there has been an 89% decrease in mortality from tuberculosis in the period 1919 to 1958. The largest yearly decrease (27.8%) occurred in 1952 with the introduction of isoniazid. In other years there was a decrease of 3 to 15%. The decrease has been more rapid for tuberculous meningitis than for pulmonary tuberculosis, and the difference has become more pronounced between 1951 and 1958, or since the introduction of isoniazid. The decrease in the case fatality rate of tuberculous meningitis was 87%, while that of pulmonary tuberculosis was 57.5%. This difference was attributed to the fact that the patient with pulmonary tuberculosis often interrupts the treatment. The decrease in death rates was especially marked among young patients. It was 89% in infants under 1 year of age; 98.9% in the 1 to 19 year age group; 98.3% in the 20 to 24 year age group; 94.9% in the 25 to 29 year age group; and 82% in the 45 to 49 year age group. In patients over 50 years of age the decrease was less marked, being 47% in the group aged 65 to 69. After the age 70 the rate showed a slight increase.

The death rate from tuberculosis was higher among men than among women. As early as 1930 the rate was 113 per 100,000 inhabitants for women, and 163 per 100,000 for men. In 1957 these rates were 13 and 37 per 100,000 respectively. The cause of this increasingly marked difference is found in the elimination of the high death rates represented by young women dying of galloping consumption and pregnant women dying of tuberculous cavitations.

Male Sterility.—H. Bayle and C. Gouygou (*Journal d'urologie medicale et chirurgicale*, vol. 64) reported a series of 2,000 cases of sterility in men, emphasizing the role of vascular disorders in the alterations of spermatogenesis. Hydroceles cause disturbances by interscrotal compression, often aggravated by pachyvaginalitis. Varicoceles cause testicular disturbances that are aggravated by the use of suspensories. The authors treated this condition by resecting the scrotum rather than the veins. They also considered cryptorchism to be secondary to spontaneous vascular disorders. Postoperative vascular disorders also play a role in the disturbances of spermatogenesis. Inguinoscrotal operations are among the main causes. The ligation or resection of an artery and the compression of the vasculonervous tissue of the spermatic cord during a herniorrhaphy may cause testicular lesions. Puncture of the epididymis as well as the blind technique of infiltrating the cord with procaine are disapproved of by the authors, because they lead to azoospermia. On the other hand, operations that damage a spermatic artery, ablation of an epididymal cyst without subsequent epididymodeferential anastomosis, and microtraumas of the globi play an etiological role.

In some patients with oligospermia or azoospermia, biopsy specimens revealed vascular fibroses involving the arterioles and precapillaries of the deferential tunics. In some the arteries and intralobular veins were also damaged. On the other hand, modified vessels were found, with a soft longitudinal subendothelial musculature.

I. Bertrand (*Revue française de gynécologie et d'obstétrique*, April, 1959) reported that according to certain statistical data, in 50% of the sterile couples the cause is male sterility. In half of these men, sterility is caused by obliteration of the excretory tract. The origin is mainly tuberculous or gonococcic, and it may be treated by a single-stage operation which establishes the diagnosis and corrects the defect. Two types of operation are used: the "trabucco" which consists of inserting the vas deferens inside the epididymal head, and side-to-side anastomosis between the vas and the epididymis.

In male sterility of a secretory origin, hormonal treatment is indicated because of the role played by the androgens and estrogens in spermatogenesis. Androgens in large doses (up to 2.7 Gm.) inhibit spermatic secretion by causing hypersecretion of the pituitary. In some patients this therapy may aggravate the oligospermia. Testosterone is given in a stimulating dose (5 mg. given orally or 25 mg. intramuscularly every two or three days for three months). The administration of 0.2 mg. of diethylstilbestrol daily for two weeks also has a stimulating effect. In patients with congenital or acquired hypogonadism, therapy with pituitary gonadotropins is indicated.

Venereal Disease.—P. Durel (*La vie médicalé*, January, 1959) stated that in France, in 1957, 1,348 new cases of syphilis were reported, compared with 15,454 in 1946. The decrease in the morbidity rates started with the advent of penicillin in 1937. After 1955 a slight increase has been reported in the incidence of primary and secondary syphilis. In 1955 the number of cases reported was 1,156; in 1956, 1,452; and in 1957, 1,348. Penicillin is still effective against this disease. Persistence of positive serologic test results is not necessarily a sign of active syphilis. Antibodies may persist for the rest of the patient's life, even after he is cured. On the other hand, the author believes that the few known cases of neurovisceral syphilis should not be attributed to the penicillin treatment. If penicillin is given when the lesions of the neuroaxis are already present, these lesions may continue their course even if the treponema is no longer there. The incidence of gonorrhea has decreased by almost 50% since the beginning of the antibiotic era. About 29,900 cases were reported in 1946, and in 1957 only 15,267. The author urged measures to detect the infected partners who are a source of contagion and who ignore their disease. Nongonococcic urethritides are more frequent than gonococcic. The presence of Trichomonas vaginalis seems to be the causative agent in 10 to 20% of these cases. In other urethritides of unknown origin tetracycline cures about 60% but recurrences are often observed.

GERMANY

Carcinoma of the Vocal Cord.—Hoarseness lasting longer than three weeks should arouse suspicion of a larygeal carcinoma. This diagnosis is confirmed by biopsy. The prospects for cure (around 80%) are equally good with resection of the vocal cord, x-ray, or radium treatment. Appropriate application and skillful combination of the three methods make it possible to save the larynx of the remaining 20%, frequently for a long time. The radium treatment should be tried first. If it fails, chordectomy should be performed. This cures some of the radium-resistant patients. Relapses are treated by the radiologist only if the histological findings indicate probable sensitivity to radium. If this fails, hemi or total extirpation must be performed. A.

Herrmann of Munich (*München. med. Wchnschr.* 101:1556, 1959) believed primary x-ray treatment of these patients to be a mistake. In his opinion, the radiologist should refuse to accept such patients for x-ray treatment if the other possibilities are feasible, because he thereby destroys in the 20% who are not cured initially a plan for treatment which has proved its value and which offers the possibility to the patient of preserving his larynx for good or at least for a long time. By way of deliberate action, it is possible to preserve the larynx of a patient with cancer for 10 years before having to finally perform total extirpation.

Carcinoma of the Larynx.—On the basis of a series of 334 patients with carcinoma of the larynx, the effectiveness of x-ray irradiation for the treatment of the carcinoma of the larynx was studied by F. Wachtler (*Strahlentherapie* 109:343, 1959). Of 216 patients treated by irradiation only, 82 patients (38%) lived longer than five years after the onset of treatment without evidence of recurrent carcinoma; 118 patients were treated by partial or total laryngectomy and treated with irradiation after operation. Of these 45 or 41% survived five years without evidence of recurrence. Of those with tumors of the vocal cord the five-year survival rate without evidence of recurrence was 46%. The prognosis of irradiated subglottic tumors was unfavorable. Permanent cures were rare. Supraglottic tumors had a five-year cure rate of 23.5%. Old age diminishes the chances of cure. The prognosis in those with undifferentiated carcinomas was better than in those with differentiated tumors. The main complications of radiotherapy of the larynx included perichondritis, early radiation-induced edema, pneumonia, and hemorrhage caused by erosion of ulcerated tumors, and radiation-induced anorexia.

Ventricular Septum Defect.—Among the most frequent congenital heart anomalies are the ventricular septum defects (VSD). Contrary to the often-voiced opinion that this is a relatively harmless condition, R. Zenker and co-worker of Munich (*München. med. Wchnschr.* 101:1541, 1959) found it to be associated with a serious prognosis. The selection of patients for operation must be based on a careful diagnosis with particular consideration of the ECG and, if necessary, the heart should be catheterized. In patients with a functionally insignificant VSD or a defect with severe pulmonary hypertension, the question of whether to operate must be carefully considered. Other cardiac defects that would complicate the VSD must be recognized preoperatively. The operative risk for an uncomplicated VSD is small if patients are selected properly and if those in whom the pulmonary vessel resistance exceeds the peripheral resistance are excluded. Of 10 patients who were operated on of whom some had special varieties of VSD and other anomalies, only one who had severe pulmonary hypertension died.

Radionecrosis of Bones.—H. Fritz of Dresden (*Strahlentherapie* 109:510, 1959) observed late radiation damages, particularly of damage of the pubic bone and the tuber ischiadicum in 53 women after deep x-ray therapy of cancer of the female genital tract. In eight cases a fracture of the anterior part of the pelvis with partial displacement of the fragments was observed. In the others there were trabecular changes of the bony structure, principally near the symphysis. In some patients local sclerosis was noted. In a number of patients spontaneous healing was observed. In only one patient was overirradiation the cause. The use of the seven-field technique was especially hazardous. Cobalt-60 irradiation appeared to be less likely to cause bony necrosis than deep x-ray therapy.

Intestinal Diseases and Spondylitis.—Observations of regular association of intestinal diseases, which are often clinically inapparent but radiologically and bacteriologically manifest, and ankylosing spondylitis suggested a connection between the two disorders, according to F. Kuhlmann of Essen (*Ztschr. Rheumaforsch.* 18:200, 1959). The exceptional therapeutic success of combined treatment with sulfadiazine in doses of 250 mg. three or four times daily and a derivative of thiosemicarbazone (Iversal) in doses of 10 mg. two or three times daily in rheumatoid arthritis and in ankylosing spondylitis before complete ossification confirmed the suspicion of intestinal causative factors.

Potassium for Digitalis Hypersensitivity.—V. Braun (*München. med. Wchnschr.* 101:1187, 1959) stated that due to the occurrence of hypersensitivity to digitalis in patients with hypopotassemia, the following vicious circle may result from digitalis therapy: An intracellular loss of potassium may occur in patients with cardiac insufficiency as a consequence of water and sodium uptake. When the administration of digitalis leads to diuresis, potassium is excreted, resulting in digitalis intolerance which leads to further loss of potassium by vomiting and diarrhea. As demonstrated in a case of digitalis intoxication, all symptoms of such intoxication can be dissipated within a few days by administration of potassium.

Antiphlogistic Drugs.—G. L. Haberland and coworkers of Elberfeld (*Ztschr. Rheumaforsch.* 18:220, 1959) stated that clinically effective antiphlogistic drugs are inactivating antibodies (they inhibit hemolytic amboceptor of sheep erythrocytes). This was demonstrated for aspirin, phenylbutazone, prednisolone, and chloroquine. A marked precipitation of sulfate polysaccharides and of nucleinic acids by chloroquine was observed. The different effect of various antiphlogistic drugs was demonstrated by the UV-erythema and UV-edema test in guinea pigs. A strong inhibition effect of chloroquine was also demonstrated in rats. The same was shown with fibroblast cultures of various origin. The experimentally demonstrated differences of action of various antiphlogistic drugs led to the development of a combination of aspirin, prednisone, and chloroquine (Elestole), which is helpful in the treatment of chronic rheumatic diseases.

Poliomyelitis Vaccine.—H. Kleinschmidt (*München. med. Wchnschr.* **101**:1177, 1959) stated that, after it was certain that under careful production and control the danger of administering Salk vaccine is extremely low, the protective inoculation against poliomyelitis was taken up again in the Federal Republic of Germany and in West Berlin in 1957. Priority was given to children in the second and third year of life because only little vaccine was available. In spite of sufficient amounts of vaccine and widespread publicity the number of inoculated children increased in 1958 only from 631,650 to 807,464. It is obvious that the necessity of inoculation is not yet generally accepted in wide segments of the population, due to the diminishing incidence of the disease. The effectiveness of the immunization was proved by the diminished incidence among those children who were inoculated in 1957, and not by the generally diminished incidence which may be due to epidemiological variations. The Salk vaccine was not entirely satisfactory, as paralytic cases have occurred and some patients in the United States have died after three injections. Cases of insufficient formation of antibody and rapid decrease of antibody were also noted. Therefore, the necessity of a fourth injection has been emphasized, as well as the necessity of improving the concentration of individual virus antigens. It is clear that the interest in a living attenuated vaccine is growing. Perhaps it is useful to start the oral administration of these viruses only after giving the usual Salk vaccine. For the time being, however, only the inactivated Salk vaccine should be used. The combination of poliomyelitis vaccine with diphtheria-pertussis tetanus immunization is recommended.

INDIA

Plasma Proteins in Malnutrition.—Achari and Misra (*Calcutta Medical Journal*, vol. 56, June, 1959) estimated the plasma proteins in patients with malnutrition. They used the ultraviolet spectrophotometric method of Waddell and Hill. Estimations were made before and after treatment to evaluate the method. Patients with edema due to malnutrition were selected for this study. To obtain normal values random selections were made from subjects of different ages and sexes. The total plasma proteins and the albumin fraction showed marked reduction compared to normal in patients with all grades of edema. This reduction was found to be statistically significant, while the plasma globulin fraction showed no significant reduction. Nine patients were given blood transfusions twice a week to see the effect of such treatment. The total plasma proteins and the plasma albumin figures showed a significant improvement after this treatment indicating that blood transfusions are effective in replacing the plasma proteins. There was also associated clinical improvement.

Nystatin for Candidiasis.—S. Rajagopalan (*Medioscope*, vol. 2, 1959) treated a series of 31 patients who had cultures positive for candidiasis with nystatin. Of these, 18 had perlèche, 3 had vulvovaginitis, 2 had thrush, 4 had nail infections, 2 had interdigital candidiasis, 1 had intertrigo, and 2 had nutritional dermatitis involving the scrotum. An ointment containing 100,000 units of nystatin in 1 Gm. of hydrocarbon gel was applied twice daily to the affected part. Except for four patients with perlèche and those with nail infections and interdigital candidiasis all were completely cured. Patients with nutritional dermatitis were the only ones whose treatment was supplemented with vitamin B_{12} or vitamin B complex. The nystatin was well tolerated and there was no instance of sensitivity to the drug or the base. The treatment was administered for a period of 10 to 20 days. The poor response in nail infections and interdigital candidiasis may have been due to occupational trauma.

17-Ketosteroids in Malnourished Children.—Chakraborty and Chatterjee (*Calcutta Medical Journal*, vol. 56, July, 1959) collected 24-hour samples of urine from children aged between 1 and 8 years. These children did not have any recognizable disease except congenital defects such as a cleft lip or palate and none of them was given any drug which might have an excitatory or depressive influence on androgen formation by the adrenal cortex. Fluid intake and output were recorded and were within normal limits. A series of 75 malnourished children in whom there was no other recognizable disease were then similarly studied. These children had lost at least 40% of their expected body weight as determined by age, sex, and height. They were listless. The subcutaneous fat was almost absent and 50% had some evidence of avitaminosis-A. They had varying degrees of pallor and anemia. The serum sodium and potassium levels were determined in all the 75 but the 17-ketosteroids were determined only in 5 due to the difficulty in collecting 24-hour urine samples.

The serum sodium and potassium levels and the urinary 17-ketosteroids were all lower than normal in malnutrition. The normal figure for urinary ketosteroids was 0.84 mg. in 24 hours (range 0 to 1.18). In malnutrition, the average value for urinary

17-ketosteroids in 24 hours was 0.025 mg. (range 0.001 to 0.05). The low serum sodium level and the small excretion of ketosteroids in malnutrition represented hypofunction of the adrenal cortex. Earlier work by one of the authors had shown that patients who had malnutrition and a low blood chloride level developed edema. The adrenals in these patients presented varied findings. The zona reticularis was somewhat irregular in arrangement with big sinuses which were also seen in the medulla. As a low serum sodium level is associated with a low serum chloride level, the present investigation gave further support to the view that edema in malnutrition is associated with low blood chloride levels and hypofunction of the adrenals.

Medical Examination of School Children.—V. B. Athavle (*Indian Journal of Child Health*, vol. 8, August, 1959) analyzed the results of medical examination of 1,004 school children aged 3 to 18 years. The different milestones in the growth of these children were, on the whole, comparable with those of Western children. In one group of 118 children 110 had been vaccinated against smallpox in the first year of life. Three had had the disease. In one repeated attempts at vaccination had proved unsuccessful. The incidence of other immunizations was low; nine children gave a history of diphtheria and seven of pertussis. Of the 1,004 children 102 had been operated on; 78 of the operations were tonsillectomies. The average height and weight of these children was well below that of white American children and the average head circumference was 1 in. less, the chest circumference 3 in. less, and the abdominal circumference 2.5 in. less. Although the children lagged behind in physical growth as compared to Western standards, their development as determined by eruption of first deciduous tooth and appearance of secondary sex characters was comparable with that in Western children.

Kerosene Poisoning in Children.—Mukherji and Sur (*Indian Journal of Child Health*, vol. 8, August, 1959) stated that kerosene is used for lighting and cooking and is an essential commodity in urban households where there is no electricity and in rural areas. Kerosene is thus a common cause of accidental poisoning. A series of 27 cases of kerosene poisoning in children was analyzed. Of these 22 were aged 2 years or less (range 10 months to 12 years) and 23 were boys. The average elapsed time between ingestion of the kerosene and arrival at the hospital was four and one-half hours. The two patients who died were brought to the hospital within 30 minutes, but in most the time interval was related to the prognosis and those who developed pulmonary complications were admitted after a lapse of many hours. More than half of the patients were well after 48 hours, the average stay in the hospital being 3.2 days. The quantity taken was not definitely known in any case but on an average varied from a mouthful to 2 oz. There was no history of kerosene poisoning in other children of the family and the same child never was admitted a second time for this condition. The most common symptoms were vomiting, cough, tachycardia, thoracic complications, fever, and drowsiness. An odor of kerosene could usually be detected on the breath. Gastric lavage with saline solution or water was performed on 23 patients. All were given penicillin and sulfonamides parenterally. Some received broad-spectrum antibiotics. Oxygen was given to seven children. The two deaths were due to depression of the central nervous system.

Chloroquine for Lepra Reactions.—G. Ramu (*Journal of the Indian Medical Association*, vol. 33, Aug. 16, 1959) observed eight patients with lepromatous leprosy who had a lepra reaction. Two of these were being treated by diaminodiphenylsulfone (DDS) and isoniazid while others received DDS alone. One of the patients had amebic hepatitis complicating a severe lepra reaction. Chloroquine was given for the amebic hepatitis, and, in addition to improvement in the hepatic condition, the skin reaction also subsided. Chloroquine was therefore given to the other seven patients with lepra reaction. All of them showed symptomatic relief with disappearance of fever and the subsidence of inflammatory skin lesions, arthritis, and orchitis. The author recommends a dose of 250 mg. thrice a day for one week and later 250 mg. twice a day for another two weeks.

Palpable Liver in Normal Children.—K. J. Vyas (*Indian Journal of Child Health*, vol. 8, August, 1959) stated that, although enlargement of the liver in children is associated with many common diseases, such enlargement does not necessarily suggest disease. The author examined 715 healthy neonates, infants, and children and found a palpable liver in 155. The palpability showed no definite relation to the nutritional or social status of the child. The edge of the liver was always rounded and the consistency soft without any degree of firmness. An enlargement extending more than 9 cm. below the costal margin with a sharp lower edge and firm consistency should be regarded with suspicion.

Hepatic Coma.—P. L. Wahi and co-workers (*Indian Journal of Medical Sciences*, vol. 13, August, 1959) treated a series of 30 patients with hepatic coma. They were between 12 and 60 years of age. Fifteen had acute and the rest had chronic liver diseases. The latter included 14 with cirrhosis and one with secondary carcinoma of the liver. The acute diseases included infectious hepatitis, alcoholic hepatitis, severe anemia, and postoperative cholangiohepatitis. Jaundice was present in all patients, with the serum bilirubin ranging between 2.3 and 16 mg. per 100 ml. It had no relation to the depth of coma and its depth in patients with infectious hepatitis was of no prognostic significance. The jaundice was less deep in patients with cirrhosis than in those with infectious hepatitis, yet all of the former except one died while of the latter group even those with high serum bilirubin values survived. Although jaundice is uncommon in patients with portal cirrhosis, all those with terminal cholemia showed moderate jaundice at the time of admission. The depth of the coma also had no relation to the termination.

In chronic cases, it went on deepening while in acute cases patients recovered completely even after prolonged and deep coma. The prognosis was, on the whole, worse in the chronic cases. Treatment consisted of hypertonic dextrose therapy, dextrose in saline solution intravenously, or glucose and fruit juices by mouth, avoidance of proteins and lipotropic factors (proteins being added gradually during the recovery period), vitamins, broad-spectrum antibiotics (preferably tetracycline by mouth), and corticoids (orally or by injection). Glutamic acid was of little if any value. Supportive treatment in the form of fresh small blood transfusions was of great help. Morphine and barbiturates were avoided, paraldehyde being the sedative of choice. Mortality was maximal in the chronic group and lower in the acute cases. The onset of cholemic symptoms in portal cirrhosis always suggested fatal termination, although the nutritional status of these patients and those with infectious hepatitis was about the same. The latter had a 50% chance of recovery.

Treatment of Leprosy in Villages.—Belgian experts engaged in a leprosy eradication campaign have found that the incidence of the disease among women in southern India is comparatively lower than in men but, once infected, women are more difficult to cure. They believe that this low incidence is not due to any difference in physiological conditions between men and women but to the fact that women in this country have better mechanical protection against contamination. Thus, they are always covered, even at night, while men are usually inadequately clothed. In other countries both sexes are either adequately clothed or not at all, as in Africa. The mechanical protection is not available to children, as they usually go naked, and in their case the pattern of incidence is different, girls being more vulnerable than boys. The experts have recommended that, as leprosy is mostly a rural disease, it should be attacked at the village level, particularly in India with its predominantly rural population. They have also recommended domiciliary treatment.

Transaminase Activity in Neuromuscular Diseases.—Mathur and Gahlaut recorded the serum glutamic oxalacetic transaminase (SGO-T) activity in 15 patients with muscular and neuromuscular disorders (*Journal of the Indian Medical Association*, vol. 33, Sept. 1, 1959). The estimations of the SGO-T activity were repeated at weekly intervals so as to obtain two or three readings for each patient. The mean SGO-T activity in 25 normal persons was 28 units per milliliter (range 15 to 40). The level remained raised in all these patients throughout their stay in the hospital. There was no significant correlation between the age of the patient, the duration of the disease, and the level of SGO-T activity. All had atrophy of some of their muscles. SGO-T activity was normal in three of the four patients with motor neurone disease and in postpoliomyelitis atrophy, while it was moderately raised in one patient with motor neurone disease and in the patient with caries of a cervical vertebra. This estimation can be used to diagnose muscular atrophy in the early stages or in unusual forms of the disease. A raised SGO-T activity, when other causes of raised SGO-T level such as cardiac and hepatic necrosis can be excluded, would confirm the diagnosis of myopathy. In this series, all patients with myopathy had raised SGO-T activity, in contrast to only two patients with neurogenic muscular atrophy.

Chronic Manganese Poisoning.—Berry and Bidwai (*Neurology*, vol. 7, April-June, 1959) made a survey of the underground workers in some of the manganese mines and reported a series of 15 such workers who had chronic manganese poisoning. Usually the first symptom was difficulty in going downhill in the mine. This was followed by instability and weakness while doing heavy work. The voice became softer, and later there was difficulty in walking on a level surface. The general health was usually unaffected. The mobility of facial expression was diminished and nine patients exhibited the so-called manganese mask. Five had a permanent grin. Movements were slow and irregular and became more so with fatigue. Four had an accelerating gait and nine a shuffling gait. Speech was monotonous and low in volume except in one patient. It was indistinct and thick in four, who also had stuttering and sudden blocks in speech. The single most characteristic feature was the spasmodic laughter, which was easily provoked, uncontrollable, was accompanied by drooling, and ended in a whoop. The patients themselves recognized it as abnormal and complained about it. Clonic torticollis was the chief symptom in one patient and insomnia in another. Deep reflexes were present in all and brisk in five. Ankle and patellar clonus were found in one patient with spastic rigidity. Tremor was not common except in the protruded tongue.

Air encephalography revealed the presence of definite cortical atrophy in one patient and probable frontal cortical atrophy in another. Although some complained of numbness and diminished pain sensation, involvement of the sensory system was doubtful. One patient showed slight pigmentation of the anterior surface of the cornea. The sputum did not contain manganese bodies. Most patients had a mild leukopenia with relative lymphocytosis.

The disease remained stationary during the period of observation of over a year. One of the severest cases developed in a miner within one year of his starting work in the mine. Treatment with diphenhydramine, caramiphen, edathamil, and calcium-disodium did not lead to any improvement. The neurological lesion in chronic manganese poisoning involves the basal ganglions, frontal cortex, and occasionally the pyramidal system. The authors believe that a survey of all the manganese mine workers in the country will reveal many more cases of chronic poisoning.

Serum Cholinesterase and Other Levels in Amebiasis.—Kasliwal and Sogani (*Journal of the Indian Medical Association*, vol. 33, Aug. 1, 1959) studied the serum cholinesterase, alkaline phosphatase, and serum protein levels as these became abnormal in patients who had amebiasis with liver derangement. Such other liver function tests as icterus index, van den Bergh, thymol turbidity, and colloidal gold reaction showed no significant deviations from the normal. A series of 30 patients was studied. Of these 11 had no hepatomegaly or a slight nontender hepatomegaly, 16 had a tender enlarged liver, and 3 had an amebic abscess in the liver. The serum cholinesterase level was depressed in 27.2% of the first group, 56.2% of the second group, and 100% of the third group. The serum alkaline phosphatase level was within normal limits in groups 1 and 2 and high in 66.7% of group 3.

The mean values of total serum proteins were slightly less than normal in all, but these changes were not significant. The mean albumin level was less than normal in group 1; still further lowered in group 2; and lowest in group 3. The mean alpha-1 globulin level showed slight increase in group 1 and was high in the other groups. The alpha-2 globulin level showed an insignificant fall in group 1 but in the other two it showed a definite rise. The mean beta globulin level was insignificantly reduced in groups 1 and 2 but insignificantly raised in group 3. The mean gamma globulin level was raised in all but more in groups 2 and 3 than in group 1. The albumin-globulin ratio showed corresponding alterations. The values showed a tendency to return to normal after treatment.

The changes in the different serum fractions showed no relation to alterations in serum cholinesterase and alkaline phosphatase levels. A depressed cholinesterase level in patients with proved amebiasis has been suggested as a sign of hepatic involvement. It would be of value in patients with enlarged tender liver, fever, and leukocytosis. The fall in serum cholinesterase level in the patients in this series varied fairly consistently with the severity of the liver involvement. Changes in alkaline phosphatase occurred only in those with large amebic abscesses. The changes in serum protein fractions (hypoalbuminemia, hyper alpha-1 and alpha-2 globulinemia, and hypergamma globulinemia) were most marked in patients with tender livers and amebic abscesses. These changes may partly be due to deficiency of protein and presence of infection, but liver derangement is also a contributory factor.

Venous Air Embolism.—D. N. Shivpuri and coworkers (*Journal of the Indian Medical Association*, vol. 33, Aug. 1, 1959) stated that air embolism can occur during various procedures and is associated with a high case fatality rate. Usual resuscitation measures often fail, since by the time symptoms appear a lethal amount of air has already entered the right heart. The authors experimented on dogs to discover a sign of air embolism before the development of symptoms so that treatment could be started early enough and further entry of air prevented. Air was injected into the femoral vein at the rate of 0.5 cc. per second and the heart was auscultated continuously throughout. Changes in heart sounds and symptoms were noted simultaneously in relation to the timing and the amount of air injected into the vein. At 10 to 15 seconds, the sounds became metallic and resonant in character and the rate started increasing. At 20 to 25 seconds, the sounds became drum-like and this was designated as the "drum sign," the appearance of which was taken as pathognomonic of venous air embolism as the sound is pronounced and striking. The heart rate further accelerated. At 30 to 40 seconds, the systolic churning murmur described by earlier workers appeared, which replaced the heart sounds completely at 50 to 60 seconds. The first clinical symptoms appeared at 40 to 50 seconds in the form of groaning or convulsions.

Thus, the first clinical symptom appeared about 20 to 25 seconds after the appearance of the drum sign. The groaning or convulsion appeared when 1.5 to 2 cc. of air per pound of body weight had been injected but the drum sign appeared when only 0.7 to 1.0 cc. of air per pound of body weight had entered the circulation. It took twice as much air and twice as much time for development of symptoms as for the appearance of the drum sign. About 4.4 cc. of air per pound of body weight was required to produce death in dogs when injected at the rate of 0.5 cc. per second. Thus, about 500 cc. of air would be required to cause death in a man weighing 125 lb. (56.7 kg.) if the rate of entry of air into the venous circulation was the same as in these dogs.

Tropical Splenomegaly.—S. P. Basu (*Journal of the Indian Medical Association*, vol. 33, Aug. 16, 1959) made radiologic studies of 59 patients with tropical splenomegaly due to malaria or intrahepatic and posthepatic portal obstruction. Splenoportography was used to visualize the splenic and portal veins after percutaneous injection of a dye directly into the spleen. Untoward reactions sometimes occurred. The immediate reactions included pain in the shoulder, dilatation of the pupils, sensation of constriction in the chest, thirst, vomiting, and urticaria which were transient. Late reactions were manifested by perisplenitis, pleurisy, and sometimes referred pain without visualization of the splenoportal tract due to faulty injection of the dye between the spleen and its capsule.

In postmalarial splenomegaly in the early stage when there are hardly any changes histologically, the dye was found to be uniformly distributed and the branches from the splenic hilum forming the vein were clearly seen. Ramifications of the portal vein in the liver substance were well visualized while the splenic and portal veins were slightly dilated with no evidence of collateral vessels. In the second stage with enlargement of liver and spleen and degenerative changes with cellular infiltration in the liver, but no fibrotic change, the splenic and portal veins showed marked dilation and tortuosity but no collateral vessels. The portal channels were seen better in the right than in the left lobe.

In the later stages when there were secondary fibrotic changes in the liver and portal hypertension, there was wide dilatation of splenic and portal veins and formation of collateral vessels. The finer branches of the portal radicles in the liver substance were not seen and the larger ones were distorted and irregular. The passage of the dye was sometimes obstructed at the porta hepatis. In intrahepatic portal obstruction, similar changes were seen, but the spleen was less enlarged and the splenoportal veins therefore not so grossly dilated and tortuous. In extrahepatic obstruction, there was sudden obstruction to the passage of the dye and neither the splenic nor the portal vein were visualized. Collateral veins could be seen. Swallows of barium were given to 60 patients and esophageal varices were seen in 21, of whom 17 gave a history of hematemesis; 6 showed no varices although they had previously had hemorrhages. Examination of 15 unselected patients with massive spleens was made with use of full barium meal. The stomach was seen pushed to the right and in one there was varicosity in the stomach in addition to esophageal varices. The descending colon was pushed to the right. Splenectomy was followed by return of the stomach to its normal position.

Intravenous pyelography was made in 10 patients. The left kidney was not well visualized. It was enlarged and displaced downward. The dye was poorly concentrated and clubbing of the calyces was evident. After splenectomy, the position and function of the left kidney were restored. Roentgenograms of the gallbladder without dye in 10 patients showed biliary calculi in three. Cholecystography in five patients showed poor concentration of the dye. Roentgenograms of bones revealed coarse bony trabeculation in the flat bones and osteoporosis in the small bones of the hand. Superficial abdominal venography was done by injecting dye into the veins of the abdominal wall. Injection of the superior epigastric vein did not give much information, but injection into the inferior epigastric vein brought out the iliac vein of the affected side and its communication with the opposite vein. The epigastric vein was much dilated and tortuous.

Retropubic Prostatectomy.—S. P. Srivástava (*Journal of the Indian Medical Association*, vol. 33, Aug. 16, 1959) performed retropubic prostatectomy on a series of 40 patients aged 31 to 80 years. Patients with a thin or medium build and no severe kidney dysfunction and who were fit for a one-stage operation were subjected to the retropubic procedure. A preliminary cystoscopy, routine catheterization to estimate residual urine, and cystography were not routinely performed as they are likely to cause irritation and to predispose to infection. Most of these patients had retention of urine. They were relieved by insertion of an indwelling catheter. Irrigation of the bladder was done only for cystitis. Operation was performed when the blood urea ranged between 40 and 60 mg. per 100 cc.

Patients with a previous suprapubic drainage were sometimes subjected to retropublic prostatectomy but the technical difficulties were enormous, the chief being in retraction of the abdominal wall. Primary healing of the capsule was not adequate and the sutures gave way, due to leaking of the sinus in the retropubic space. Suprapubic prostatectomy was therefore preferred in these patients. Penicillin and dihydrostreptomycin were given a few days before the operation. Two of the 40 patients died, one of pneumonia and the other of shock and hemorrhage. The urine became clear on fourth or fifth day in most patients but in some slight bleeding continued for six or seven days. Suprapubic leakage occurred in four patients for more than a week but stopped gradually on insertion of an indwelling catheter. Two developed incontinence due to tear of the membranous urethra.

UNITED KINGDOM

New Diuretic.—Hydroflumethiazide, the new orally given diuretic, is related to hydrochlorothiazide, from which it is derived by substitution of the chlorine atom by a trifluoro-methyl group. The compound was discovered in a search for a diuretic without the side-effects of chlorothiazide, particularly hypopotassemia. Edmonds and Wilson (*Lancet* 2:303, 1959) found that in normal subjects hydroflumethiazide is as active as chlorothiazide in about one-tenth of the dose of the latter and causes a more prolonged diuresis of water and sodium and less bicarbonate but more chloride excretion. Its action closely resembles that of hydrochlorothiazide. In a clinical study on 30 patients, most of whom were suffering from edema due to a cardiac condition, hydroflumethiazide in doses of 50 mg. three times a day produced a satisfactory diuresis in the majority. Where it failed chlorothiazide was also ineffective, although mersalyl was occasionally effective. Failure to respond was usually associated with impaired renal function, as shown by a raised blood urea level. The hypopotassemia that occurred in some patients responded to treatment with 1 Gm. of potassium chloride three times daily. The only advantage of hydroflumethiazide over chlorothiazide was that a smaller dose was required.

Kennedy and co-workers (*Lancet* 2:309, 1959) obtained a consistent diuretic effect in 17 patients with edema of cardiac, renal, and hepatic origin treated with 200 mg. of hydroflumethiazide daily. Sodium and chloride excretion were increased threefold and fourfold respectively. The excretion of potassium was doubled. No changes in the blood levels of sodium, chloride, or potassium were observed.

Blagg (*Lancet* 2:311, 1959) compared the action of hydroflumethiazide with that of chlorothiazide in normal subjects and in patients with edema due to heart disease. In both groups the patterns of diuresis and electrolyte excretion were similar, provided effective doses of the two drugs were given. The suggestion that hydroflumethiazide is less likely to cause excessive loss of potassium was not supported by the data obtained. Potassium supplements are necessary according to Blagg if the drug is to be given for more than a few days.

Death of Sir Robert Young.—Sir Robert Young, the internationally known British chest physician, died at 88 years of age. He influenced the treatment of diseases of the lung more than any doctor of his generation and had much to do with the development of mass radiography, chest surgery, and the Institute of Diseases of the Chest in London. His medical career began when diagnoses were made at the bedside without the aid of laboratory tests and roentgenograms. In his later years, although he used these adjuncts, he could still amaze his juniors by diagnosing difficult chest cases on the history and physical examination alone. At times he complained that many patients today are over-investigated and overtreated. His patients will remember him for his courtesy, kindness, sympathy, and consideration.

Doctors as Targets.—An attack on the powers of the executive councils of the National Health Service was made in the *Medical Press* of Oct. 2. They are described as an "array of vengeful bodies." In an editorial it suggested that the Minister of Health should look again at the councils, at their constitutions, and especially their powers and practices. In many cases in which a physician is made a target of litigation, it is a case of "heads I win, tails you lose." Anybody is entitled to bring before an executive council an allegation of any sort against a doctor. No matter how frivolous, scandalous, malicious, or unfounded that allegation may prove to be, the person who has made it is entitled to walk away scot-free, even though he may have perjured himself many times.

Conversely there is no remedy for the physician, however innocent he may be. He is left only with the dubious satisfaction of telling the patient to take himself elsewhere. The case is cited of a physician fined about $150 by the London Executive Council for failing to attend a 2-year-old boy, taken ill in a car with what seemed to be a convulsion one Sunday. It was stated that the doctor was apparently not aware of his obligation to treat any patient in an emergency. The physician, however, had advised the father to take the child to a hospital where there were the facilities necessary to treat the patient. The executive council came to its decision happily unhindered by any of the inhibitions that beset a court of law.

To arrive at an adverse verdict against a physician it would be necessary to show in a court beyond reasonable doubt that the patient had suffered as a result of the doctor's action. There was no evidence in this case that the patient had suffered, and the fine was higher than that commonly exacted for more serious crimes. The power to recommend such penalties might seem great especially for a body of untutored laymen not governed by the rules of evidence. Some believe that a council should not have been entrusted with it at all. By his terms of service a general practitioner is obliged to go on demand to any emergency, real or imaginary, at the beck and call of any Tom, Dick, or Harry at any time. On what trade union, asks the *Medical Press*, would any Minister attempt to impose such terms?

Sterilizing by Irradiation.—The Atomic Energy Authority announced that a pilot plant for testing irradiation processes, such as the sterilization of medical equipment and the disinfection of packaged products, is being built. It will occupy an area of about 10,000 sq. ft. of which roughly 1,000 sq. ft. is taken up by the irradiation cell itself with its massive concrete shielding walls. To make full use of the source, which is continually radiating and decaying, the plant will operate 24 hours a day, and in this period three tons of medical products or imported animal fibers can be rendered sterile. Interlocks and control devices will be incorporated to prevent injury to the workers and to ensure the correct radiation dosage.

No Extra Fee for Hypnosis.—Doctors who help mothers in childbirth by use of hypnosis may not claim an extra fee according to a ruling by the Minister of Health. Last November the Minister approved the fee of a doctor called in to administer an anesthetic who used hypnosis, but he was a second doctor and was accustomed to use of hypnosis as part of his professional practice. The ruling referred to states that the Minister is unable to approve the payment of an extra fee for an anesthetic, whether it be hypnosis or otherwise, when a second practitioner is not employed and it is administered by the general practitioner who has undertaken to provide maternity medical service.

CORRESPONDENCE

HARVEY CUSHING

To the Editor:—On Oct. 7, 1939, Harvey Cushing whose work and personality were among the glories of American medicine, died. Cushing was the incarnation of the highest ideals in research and medical practice. When, in 1935, his "Intracranial Tumors" was published in Berlin I remember the admiration aroused by reading, in his own fascinating, modest words, the extraordinary fact that on Aug. 15, 1931, he had successfully performed his 2,000th brain operation.

The man and his work were enthusiastically described by Prof. Fedor Krause, a great predecessor of Cushing in the field of surgery of the central nervous system, through whom I received some of Cushing's papers on war injuries to the brain. From December, 1916, to April, 1918, I was military assistant at the surgical clinic of the University of Greifswald where we had to operate on many patients with brain abscesses caused by shell injuries.

Cushing was admired by all German surgeons who had visited the United States. My colleague, the late Martin Gumpert, when he left Germany for the United States in 1935, sent me his book, "The Life for the Idea," describing the lives of nine medical scientists. In the last chapter, entitled Outlook: Harvey Cushing, the Brain Surgeon, Gumpert said, "Cushing is the man who grappled the unredeemingly death-bound with a tumor in their brain by a lifelong, tenacious, systematic, ingenious effort from death. . . . He has placed his own life, the life of his assistants and helpers, the facilities of his hospital, the course of every day, the mechanism of every step in the service of this one and only thing, the operation on brain tumors. . . . Thus he won the decisive victory over death." Georg Rosen said, "It was one of the rare gracious actions of Fate that such a man as Cushing in the years of his formative growth became not only the disciple but also the friend and heir to William Osler. . . . No wonder that his extraordinary 'Life of Sir William Osler' won him not only [in 1926] the coveted Pulitzer Prize but the general applause of the literary world." Rosen pointed out that, under the influence of Osler, Cushing early developed an interest in medical history, which led eventually to his "Bibliography of Andreas Vesalius" (1934) and the superb collection of books which he bequeathed to Yale University.

My contact with Cushing originated in my own bibliophilism. I never met Dr. Cushing but from October, 1937, until his death in October, 1939, I corresponded with him. He thus honored me with 10 letters, all of which were lost in the destruction of my house in Manila in February, 1945, by the Japanese. After Dr. Cushing's death Mrs. Cushing had asked me to send these letters to Yale University Library, where photostatic copies were made. They were then returned to me in Manila. Thus at least the content of these highly esteemed letters remains alive in the Cushing Collection at Yale University. About 1937 I found in the state library in Berlin a historical sketch by Dr. Cushing of the famous anatomic theater of the Archiginnasio at Bologna. I asked Cushing for a reprint and included in my letter my historical medical papers dealing with the Nuremberg town physician Hieronymus Muenzer (d. 1508) and his great book collection, which was auctioned about 1935 in Zurich. Cushing wrote me that at that auction he had bought two of Muenzer's handwritten college notebooks from his days as a medical student in Bologna in 1480-1482. He asked for reprints of my two Muenzer papers to send to Dr. Arnold Klebs at Noyon, Switzerland, and Dr. Georg Sarton at Boston.

I was finally able to leave Hitler Germany for Manila. On the day of boarding ship in Genoa in February, 1939, I received a letter from Dr. Cushing. A few weeks later the dean of the Medical College of the University of the Philippines, the chairman of the licensing committee, told me that Dr. Cushing's friendly letter and the fact of his personal interest had removed all barriers to giving me a license to practice. I became a lecturer on medical history at the Philippine Medical College, and it was indeed sad that my second lecture, in the autumn of 1939, had to be a Cushing Memorial Lecture.

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EFFECT OF ALCOHOL ON THE LIVER

To the Editor:—In the Aug. 1 issue of The Journal, page 1671, a report to the Council on Foods and Nutrition, by Dr. Gerald Klatskin, entitled "Effect of Alcohol on the Liver," is presented as a review of the available evidence implicating alcohol as a factor in hepatic injury (chiefly cirrhosis). It discusses the statistical relationship between alcoholism and cirrhosis and the possible mechanisms whereby alcohol might cause cirrhosis. It concludes that chronic alcoholism is an etiological factor in the pathogenesis of Laennec's cirrhosis, but the mechanism whereby its effects are accomplished has not been clearly established.

Probably the most widely accepted theory to explain the action of alcohol involves its indirect effects on nutrition, the assumption being that the malnutrition is the factor which leads to the liver damage. Dr. Klatskin includes the evidence against this idea and properly concludes that "whereas the malnutrition associated with excessive drinking undoubtedly accounts for many of the effects of alcohol on the liver, other as yet unidentified mechanisms may be involved."

Other mechanisms that have been investigated are also discussed, and not surprisingly none is found to be more satisfactory in explaining the obvious but inconstant relationship between alcoholism and cirrhosis. Any explanation that is acceptable must be able to account for the statistical relationship between the two and also for the occasional case of cirrhosis in abstainers (even juveniles) and the more common absence of cirrhosis in severe alcoholics.

One possible mechanism which might satisfy these apparent discrepancies was not mentioned in this review. This concerns the possible effects of alcohol on the liver through changes in hepatic circulation. The effects of alcohol on blood vessels elsewhere are well known. The involvement of the hepatic circulation in cirrhosis is also well known. The fact that changes in hepatic circulation precede cirrhosis (Banti's syndrome) in many patients is undeniable. The possibility that they precede the liver changes in many more patients with cirrhosis, perhaps in all such patients, is not so remote as might appear at first glance in view of the relative clinical silence of uncomplicated portal hypertension. While the usual explanation of the portal hypertension considers it the result of the liver changes due to obstruction, this explanation is by no means entirely satisfactory. The possibility that the portal hypertension and the liver changes are due to a common etiological factor deserves greater consideration than has been afforded it. Certainly portal hypertension does occur without cirrhosis and not infrequently without other grossly demonstrable lesions.

Some attention has been paid to the possible role of abnormal communications between the hepatic artery and the portal vein within the liver in the pathogenesis of portal hypertension. Perhaps unfortunately this attention has been directed to it as a consequence of or secondary to cirrhosis or some other supposedly obstructing lesion and little thought given to it as a possible primary cause of trouble. While communications between the high-pressure and low-pressure systems are difficult to demonstrate, there seems no reason to doubt that they exist in the human liver. If they do exist and are functional to a degree greater than normal, possibly there might result (1) an increase in pressure in the portal venous system and (2) a diversion of arterial blood from its normal pathway to the liver cell into the portal system, this in turn resulting in hepatocellular anoxia which leads to fatty degeneration and necrosis—in other words, the stages in the pathogenesis of cirrhosis.

Alcohol, being a vasodilator, might be the factor responsible for the increase in functioning capacity of these intrahepatic arteriovenous shunts. It is equally possible that congenital variations in the capacity of the shunting mechanism might exist and be responsible for the development of cirrhosis in infants and children. Other variations in the functional capacity or physiological responsiveness to alcohol or other vasodilating influences might account for variability in the susceptibility of different livers to the development of portal hypertension or cirrhosis. A person with a greater than average shunt might develop cirrhosis without alcoholism, while one with a small or static shunt system might consume alcohol heavily and maintain a healthy liver. Many influences other than imbibed alcohol, whether dietary factors or lack of them, inhaled substances, medicaments, and allergies, might exert some influence toward the production of cirrhosis through their effect on the hepatic circulation, if this be the intermediate step being sought.

The foregoing is a highly theoretical consideration, but the lack of a better explanation for the mechanism whereby alcohol may be responsible for causing cirrhosis would seem to make it worth investigating. How it might be investigated would have to be left to those concerned with research in this field, but the use of the sensitive and accurate electronic flowmeters may prove to be helpful. By whatever means, however, if the changes in hepatic circulation associated with cirrhosis are proved to be precursors rather than consequences of the liver disease, many gaps in our understanding of this problem may be filled.

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The above comment was referred to the author of the article cited, and he has submitted the following reply.

To the Editor:—There is no denying that the precise role of alcohol in the pathogenesis of cirrhosis is still uncertain and that not all conceivable mechanisms were discussed in my paper, but the hypothesis suggested by Dr. Stephenson, that circulatory changes precede and induce the development of cirrhosis in chronic alcoholics, has no pathological or experimental evidence to support it. Certainly it has not been established that the cirrhosis found in occasional patients with congestive splenomegaly (Banti's disease) is the consequence of portal hypertension. It is true that patients develop portal hypertension in the absence of cirrhosis, but to my knowledge proof of the subsequent development of cirrhosis in such persons, by means of serial biopsy studies of the liver, is still lacking.

In a recent report of such cases (Tisdale and Klatskin: *New England J. Med.* 261:209 [July 30] 1959) there was no evidence of cirrhosis even after many years of sustained high portal pressure. In a study on dogs, Schilling and McKee (*Surgical Forum* 4:392, 1953) found that even five years after the creation of an hepatoportal arteriovenous fistula no cirrhosis developed, although the liver showed focal fibrosis of the portal triads and sinusoidal congestion, features described in the previously mentioned patients with portal hypertension in the absence of portal obstruction. Moreover, the lesions of Laennec's cirrhosis, and particularly the characteristic degenerative changes, including Mallory bodies, and the pattern of fibrosis, bear no resemblance to the changes noted in the liver of patients with known circulatory disturbances.

Dr. Stephenson's suggestion that alcohol increases arteriovenous shunting within the liver is not supported by the few direct measurements that have been made. In a study on dogs reported by Smythe and others (*Am. J. Physiol.* 172:737 [March] 1953) massive doses of alcohol did not affect hepatic blood flow, vascular resistance, or sulfobromophthalein extraction. Using much smaller amounts of alcohol in man, Mendeloff (*J. Clin. Invest.* 33:1298 [Oct.] 1954) found that the hepatic blood flow, estimated by the sulfobromophthalein method, did increase, but the extraction of sulfobromophthalein by the liver did not diminish, as might be expected if the increase in flow were due to the intrahepatic arteriovenous shunting postulated by Stephenson. Indeed, it is difficult not to agree with Mendeloff's conclusion that the increased hepatic blood flow was due to a decrease in the peripheral resistance in the prehepatic splanchnic circulation.

Gerald Klatskin, M.D.
Yale University School of Medicine
New Haven 11, Conn.

TISSUE NECROSIS

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Detailed studies, in animals, of the comparative necrotizing properties of levarterenol (Levophed) and metaraminol indicated the safety of metaraminol after injections of large doses of the undiluted agent into soft tissues (Bryant and Howard *A. M. A. Arch. Surg.* 75:1020 [Dec.] 1957). Literally tens of thousands of intramuscular and subcutaneous injections of metaraminol have been used in patients (Weil: *Minnesota Med.* 40:241 [April 1957). Not a single instance of tissue injury was observed. The recommendations made by the authors as to the dangers of intravenous infusion of metaraminol and, by implication, the danger of its subcutaneous and intramuscular administration rest on tenuous interpretation of the features of a single case. It would be unfortunate if this report were to detract from the large body of evidence indicating that the appropriate use of metaraminol by the subcutaneous, intramuscular, or intravenous route has not resulted in tissue injury.

Max Harry Weil, M.D.
Los Angeles County General Hospital
1200 N. State St.
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Edward R. Dorney, M.D.
P. O. Box 459
Atlanta 22, Ga.

ILLUSTRATED FILM REVIEWS

HOSPITAL SEPSIS—A COMMUNICABLE DISEASE

Carl W. Walter, M.D., Boston

This film is sponsored by the American Medical Association, the American College of Surgeons, and the American Hospital Association. It shows how bacterial infections are spread in hospitals and how they can be controlled. The age of antisepsis, introduced by Lister, succeeded in minimizing cross-infections. However, since the therapeutic revolution of antibiotics, our guard is down. Again, many of our hospitals are reservoirs of uncontrolled infection, now complicated by the problem of antibiotic resistance.

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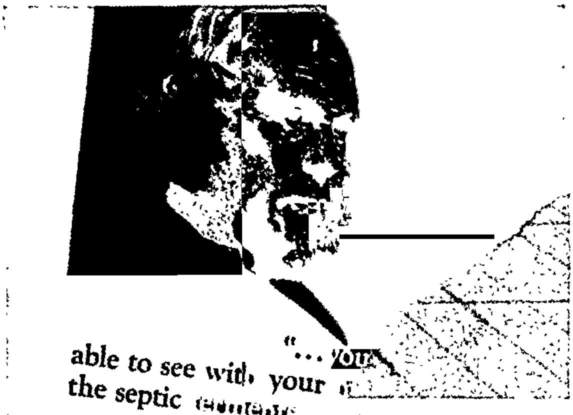
Housekeeping factors, medical care, and the human factor in the environment are all shown to be important in the spread of organisms from a single room throughout an entire hospital. Animation, time lapse, and high speed photography are used to visualize, in Lister's words, "the septic ferments," which must be controlled if cross-infection is to be checked.



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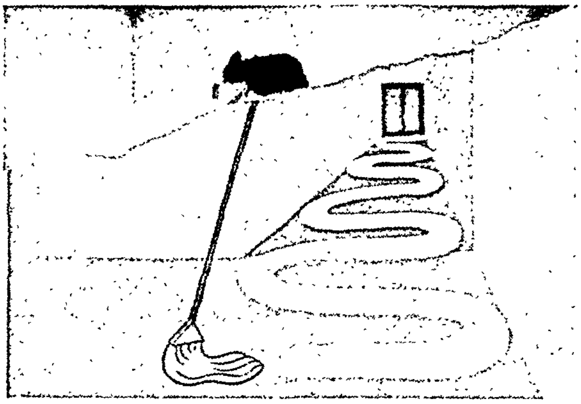

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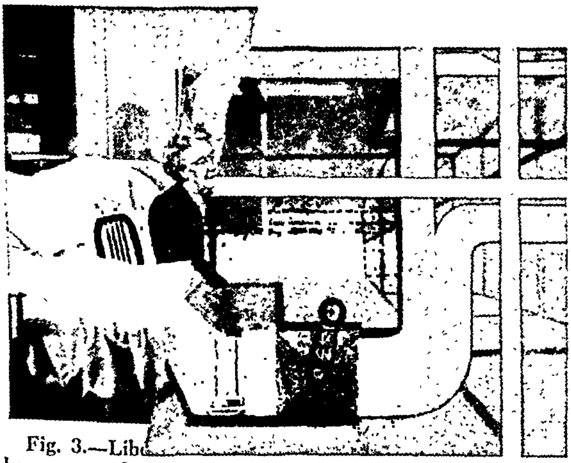

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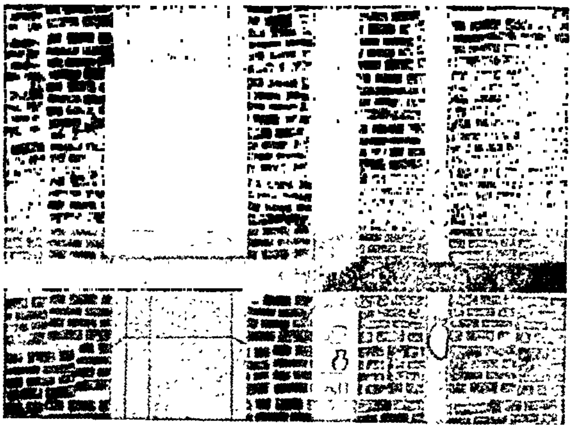

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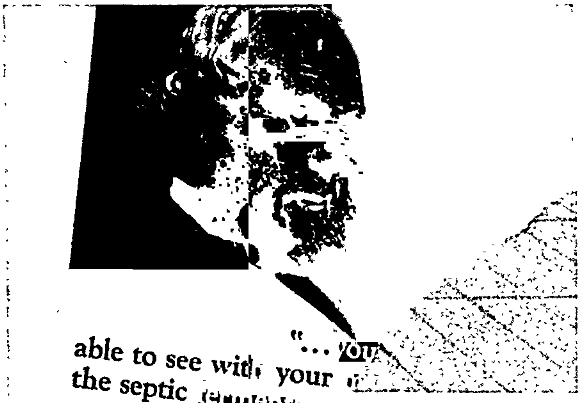
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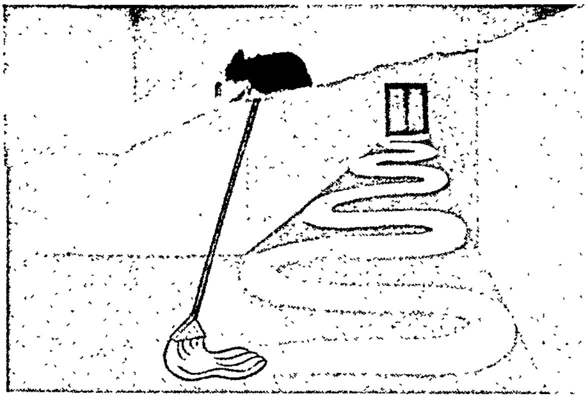

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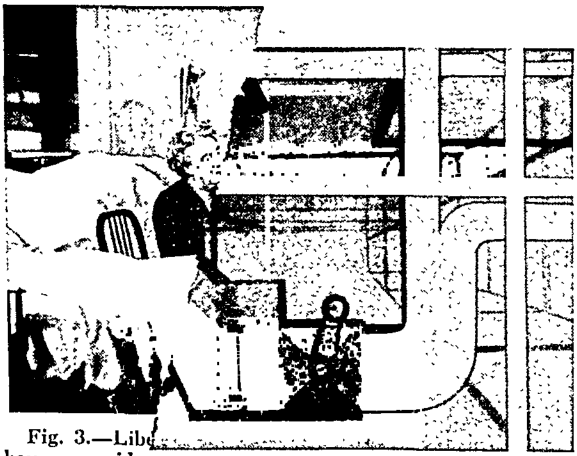

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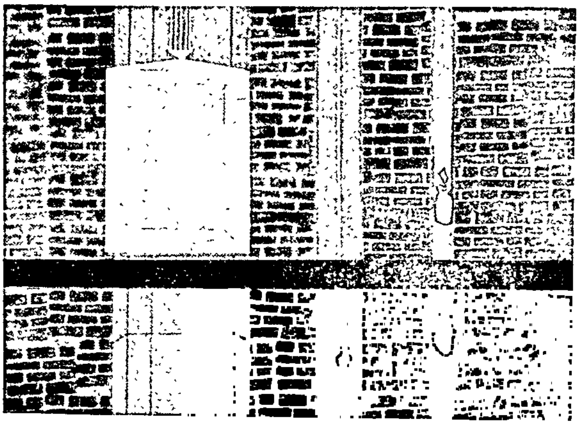

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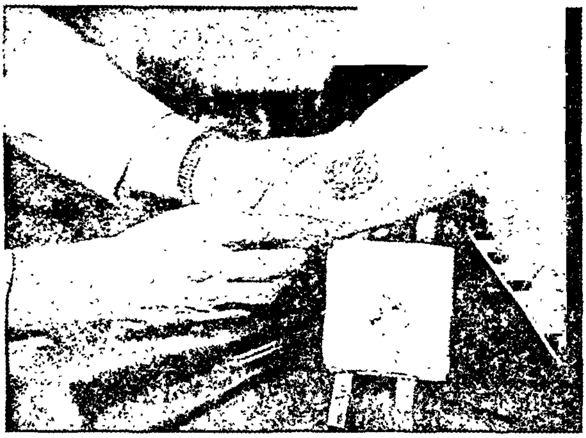

Fig. 5.—Mrs. Sarah Allen has had a 10-year history of boils. The staphylococci which caused her difficulty were alien to the hospital, and it was this fact that made her useful in tracing the spread of infection.

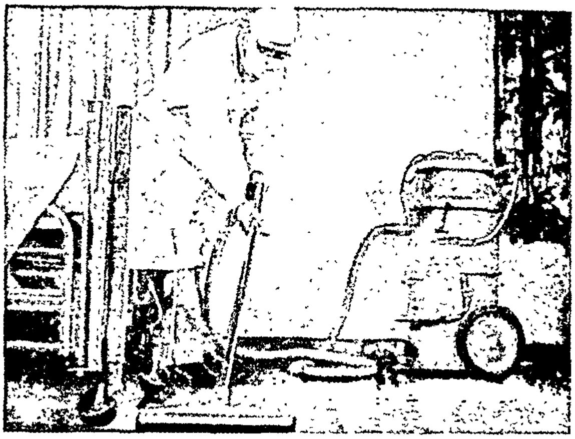

Fig. 6.—A septic environment was prepared for Mrs. Allen by thoroughly disinfecting a single hospital room.

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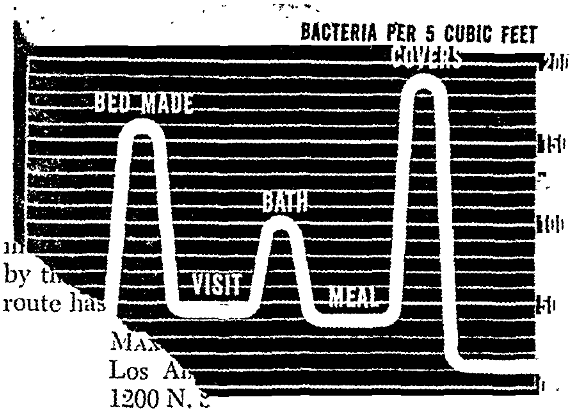

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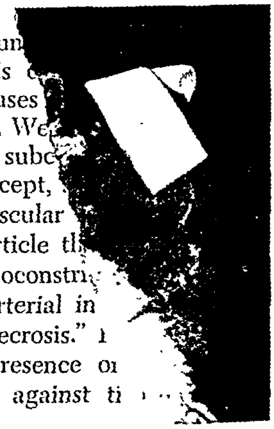

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Edward R. Dorn...
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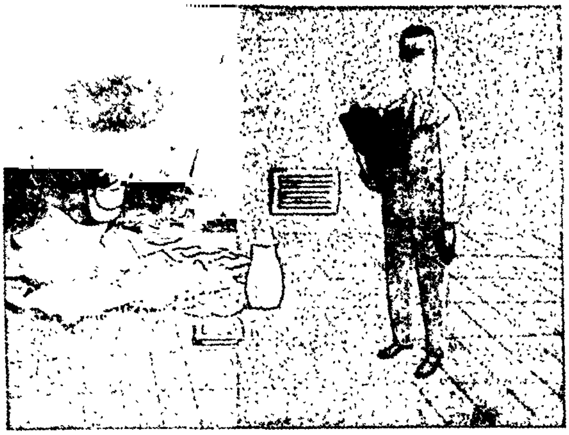


Fig. 11.—Common bacterial multipliers are soiled linen, dressings, moist soap, bedside water, the air-conditioning system, and the nasopharynx.

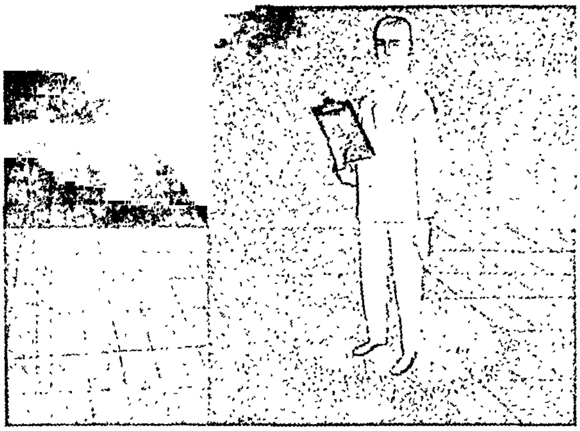


Fig. 12.—One of the many possible trails of infection is that of bacteria spread from nose to skin to clothing to floor, where they can live for long periods in the dust.

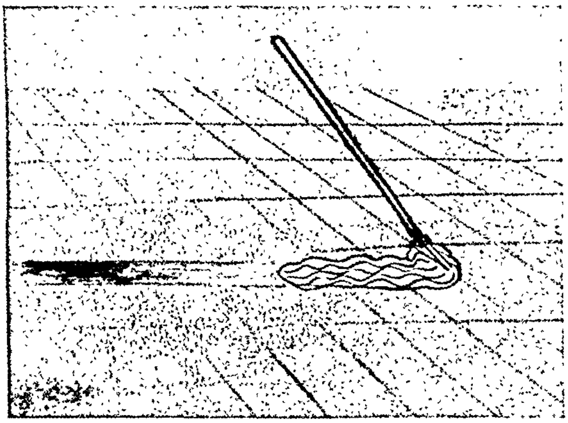
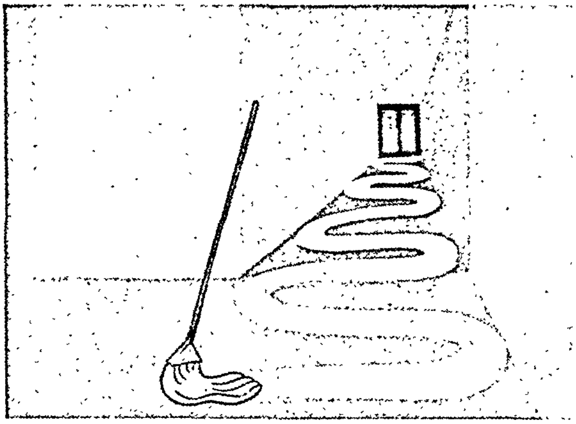


Fig. 13.—The bacteria are picked up on a mop, where overnight they multiply.



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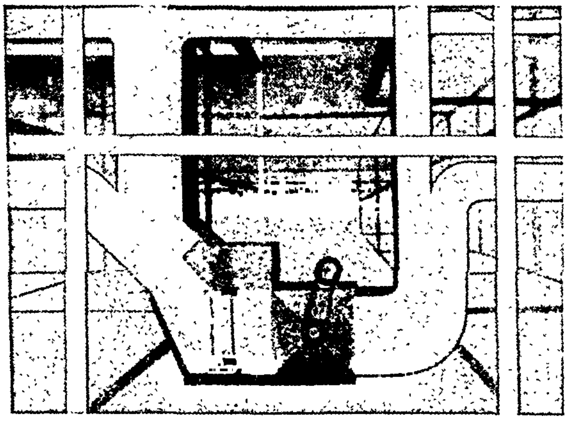

Fig. 15.—The bacteria may be carried into the air-conditioning system, where they can multiply and be further spread from room to room and floor to floor.

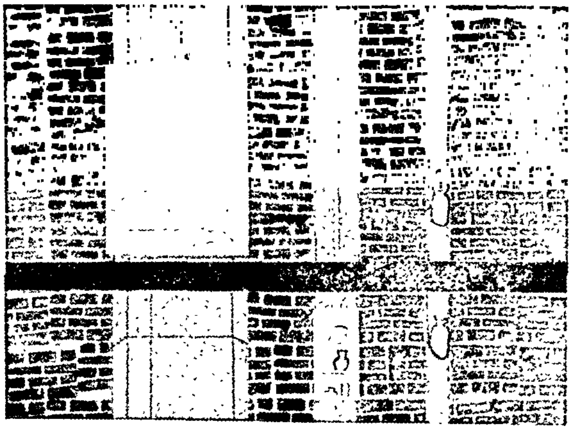

Fig. 16.—The piston action of elevator shafts, dumbwaiters, and laundry chutes do their bit in moving contaminated air around the hospital.

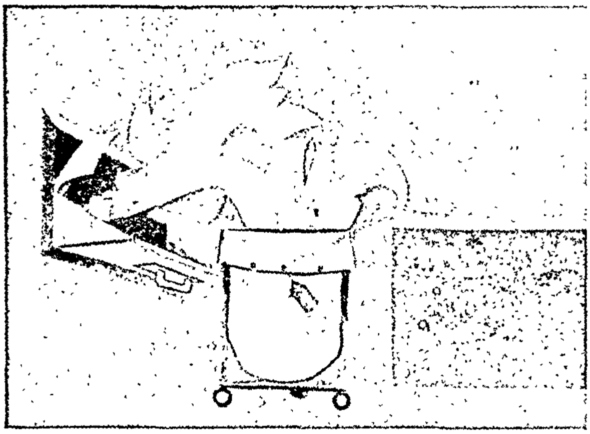

Fig. 17.—Another trail of infection may result from improper handling of laundry. Contaminated linen should never be taken from the bag or sorted before washing.

Fig. 18.—Plastic covers protect mattresses and pillows and make disinfection with a long-lasting germicide easy.

Fig. 19.—When a person drinks directly from a carafe or from a cup which also serves as a lid, saliva contaminates the remaining water and bacteria are free to multiply.

Fig. 20.—One solution is the use of disposable liners.

Fig. 21.—Vigorous enforcement of isolation techniques is necessary to confine the bacteria to the patient's room.

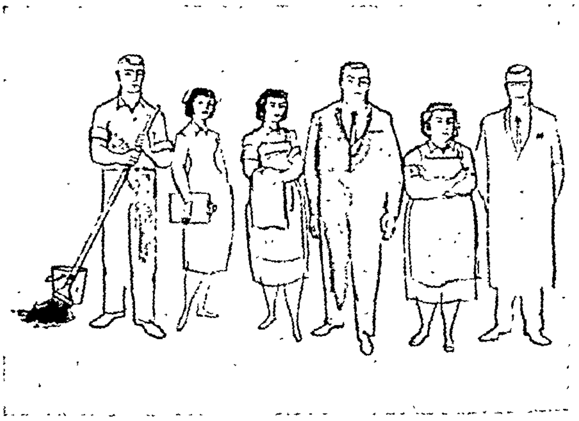

Fig. 22.—The containment of staphlococcic infection in hospitals depends on the continuous vigilance of every member of the hospital team.

MEDICAL FILM REVIEWS

Just Four Minutes: 16 mm., color, sound, showing time 25 minutes. Produced in 1958 by Sturgis Grant Productions, New York. Prepared by Lenore R. Zohman, M.D., Valhalla, New York, for and procurable on loan from Winthrop Laboratories, 1450 Broadway, New York 18.

The purpose of the film is to illustrate the team approach in a case of cardiac arrest. The picture was filmed in an apparently large hospital with excellent equipment. However, the materials and equipment shown should be available to the smaller community hospital, since cardiac arrests occur anywhere. The film begins with a differential diagnosis of the two types of arrest, namely, asystole (cardiac standstill) and ventricular fibrillation (incoordinated beats). It is an interesting fact that cardiac arrest occurs during one of every 2,000 surgical operations on patients with so-called normal hearts. A planned resuscitation program is suggested. A resuscitation cart which has all the necessary equipment is demonstrated. An interesting point concerns the electrical equipment on this cart; it is attached to one lead which can be plugged into any one of the outlets throughout the hospital. An operation is shown in progress in which entrance into the chest appears to be demonstrated on a cadaver. An actual demonstration of cardiac resuscitation in a dog is shown. Four methods of manual cardiac massage are presented and discussed. The use of the pacemaker as well as the defibrillator and the indication for each is discussed in a detailed and lucid manner. The film is excellent. Although there may be a few differences of opinion as to medicaments or time allotments, this picture can be wholeheartedly recommended. It will be particularly useful to the operating room staff.

The Early Detection and Medical Management of Ulcerative Colitis: 16 mm., color, sound, showing time 31 minutes. Prepared by Nicholas C. Hightower Jr., M.D., A. Compton Broders Jr., M.D., Henry Laurens, M.D., and Richard D. Haines, M.D., Temple, Texas. Produced in 1959 by Sturgis Grant Productions, New York, for Pharmacia Laboratories, New York. Procurable on loan from Ideal Pictures Corporation, 58 E. South Water St., Chicago 1.

The purpose of this film is to stress the importance of early diagnosis, differential diagnosis, and a suitable medical regimen for the patient with moderately active ulcerative colitis. The patient's case is presented and analyzed from the time of his initial visit to his family physician to consultations with others who have had more experience with this disease. The details of a careful, well-planned examination are outlined and conclusions about the nature of his colitis are carefully documented. The patient is brought to a clinical meeting where various aspects of the problem of ulcerative colitis are considered.

The major portion of the film centers around a gastrointestinal conference where chronic ulcerative colitis is the topic of discussion. During this conference, material is presented which includes an analysis of over 200 cases of ulcerative colitis. Sigmoidoscopy and roentgenographic examination of the colon are emphasized as procedures essential in establishing the diagnosis. Colored sigmoidoscopic pictures of the colonic mucosa are shown, depicting the various stages of the disease as seen clinically. The roentgenographic findings are divided into those in which alteration of the mucosa of the intestine occurs and those in which the changes are luminal. After this, the commonly encountered complications of ulcerative colitis are discussed. The cases are divided into two groups—those best managed medically and those best managed surgically.

The third major portion of the film is devoted to surgery. The principal therapeutic procedures that are stressed include rest, diet, sulfonamides, and supportive measures. After the conference a series of scenes show the young doctor and his patient during follow-up visits for the next year. The picture ends with the young doctor seeing his patient about a year after their first encounter. At this time the patient's disease is under control. The film is well done and particularly suitable for presentation to an audience of general practitioners or to any physicians who may see an occasional case of this disease. It also contains features interesting to the gastroenterologist and instructive to those who see patients with a variety of intestinal disorders.

NEW FILM ADDED TO A. M. A. MOTION PICTURE LIBRARY

Hospital Sepsis—A Communicable Disease: 16 mm., color, sound, showing time 27 minutes. Presented by the American Medical Association, American College of Surgeons and the American Hospital Association, with the cooperation of Johnson and Johnson. Medical supervision by Carl Walter, M.D., Boston. Procurable on loan from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film deals with what seems to be one of the more serious problems in present day hospital practice. The problem of strains of staphylococci resistant to antibiotics has engaged the attention of the medical profession, as manifested by many publications and national conferences dealing with the subject. The term "hospital sepsis" refers to the fact that the danger of this type of infection is particularly great in hospitals. The film presents the problem clearly and offers practical suggestions for correcting the difficulties. It stays away from controversial subjects about which there are differences of opinion, such as therapy, treatment of carriers, air sterilization, and the like. The film is a good review of the subject, presented in nontechnical terms. It is well organized. The photography, especially in the animated sequences, is exceptionally well done. The picture is highly recommended for physicians of all specialties, residents, interns, public health workers, and all hospital personnel.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Diagnosis and Therapy of Hypophysial Thyroid Deficiency. H. Lins and H. Zimmermann. Ztschr. klin. Med. **156**:87-93 (no. 1) 1959 (In German) [Berlin].

If the stimulating effect of the thyrotropic hormone of the hypophysis on the thyroid is abolished, secondary hypothyroidism is produced. This form of hypofunction of the thyroid is usually a symptom of insufficiency of the anterior lobe of the hypophysis. The thyroid usually retains some degree of functional activity, so that the hypofunction is never so noticeable as in primary myxedema. The authors observed hypophysial hypothyroidism in 18 of 47 patients with lesions of the hypophysis, whom they observed at a medical clinic in Düsseldorf from 1956 to 1958. This form of hypothyroidism was particularly frequent in patients with chromophobe adenoma and in those with craniopharyngioma. Generally the history and the symptoms permit a differentiation between hypophysial and thyrogenous myxedema, but occasionally great diagnostic difficulties are encountered. The thyrotropin test in combination with the radioiodine (I^{131}) method and the determination of the protein-bound iodine and of the basal metabolism are the most important aids in the differentiation.

The thyrotropin test requires a preliminary determination of I^{131} absorption. Two weeks later, 50 units of a thyrotropin extract are given intramuscularly on 3 successive days, and the I^{131} test is repeated. The difference in the I^{131} absorption before and after the thyrotropin administration is decisive. It is known that thyrotropin is effective only if the thyroid is intact. Therefore, the values remain unchanged in primary myxedema, but in hypophysial hypothyroidism iodine absorption increases under the influence of thyrotropin. An increase in protein-bound iodine and in basal metabolism after the administration of thyrotropin can be interpreted in the same manner.

The differentiation of hypophysial from thyrogenous hypothyroidism is of great therapeutic importance, because if only thyroid hormone is administered in the presence of an extensive destruction of the anterior pituitary, a latent adrenocortical insufficiency may become evident. If myxedema is definitely of hypophysial origin and signs of adrenocortical insufficiency exist, the authors advocate preliminary treatment with testosterone and cortisone before substitutional therapy with thyroid hormone is begun.

Myxedema: A Reevaluation of Clinical Diagnosis Based on Eighty Cases. H. A. Bloomer and L. H. Kyle. A. M. A. Arch. Int. Med. **104**:234-241 (Aug.) 1959 [Chicago].

The charts of all patients discharged from the Georgetown University Hospital and outpatient clinic, in Washington, D. C., with a diagnosis of primary hypothyroidism during the period 1947-1957 were reviewed. Unequivocal clinical and laboratory evidence of thyroid failure, coupled in most cases with clear-cut response to replacement therapy, was present in 80 cases. These 80 cases were analyzed as to mode of onset, symptomatology, pertinent physical features, and laboratory abnormalities. There were 69 female and 11 male patients whose ages at the time of diagnosis ranged from 16 to 73 years. Of these 80 patients, 44 were presumed to have idiopathic atrophy of the thyroid. In another 19 patients, thyroidectomy had been performed from 3 months to 30 years prior to the diagnosis of myxedema. Thirteen patients had goiter; in 6 of them open biopsy revealed Hashimoto's struma, and in 1 Riedel's struma. Myxedema developed after external irradiation to the thyroid in 2 patients and followed radioiodine (I^{131}) therapy in 2 others.

Despite progressively more accurate thyroid function tests, clear-cut clinical myxedema often goes unrecognized. The presenting complaints in myxedema are often nonspecific. However, the leading symptom in this series, paresthesia of the extremities, was of sufficient severity and frequency to be of considerable diagnostic import. The most frequent and probably the most specific confirmatory sign was slow relaxation of the deep tendon reflexes. Significant delay in diagnosis often occurs despite frequent medical consultation. Such oversight is abetted by the patient's inadequacy as a historian and by the examiner's preconceived and often erroneous concept of the clinical picture of

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The place of publication of the periodical appears in brackets preceding each abstract.

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myxedema. A history of prior thyroidectomy significantly reduces the delay in diagnosis. The most helpful laboratory test in this series was the protein-bound iodine determination, which was abnormal in 98% of the cases. Adequate response to desiccated thyroid is a characteristic of true primary myxedema. Failure of response should suggest inaccurate diagnosis. It appears that, despite increased understanding of thyroid disease and development of more precise tests of thyroid function, thyroid deficiency is being overlooked with the same frequency as was the case a quarter century ago.

Diabetes and Pulmonary Tuberculosis. C. Stephanopoulos, E. Papadopoulos and A. Polychronides. Presse méd. 67:1389-1390 (July 11) 1959 (In French) [Paris].

Pulmonary tuberculosis is one of the complications most often seen in patients with diabetes. The coexistence of tuberculosis and diabetes presented a difficult therapeutic problem before the era of antibiotics and still does in certain cases, although the use of antibiotics has reduced the mortality of diabetic patients with tuberculosis to such an extent that it now differs little from that of nontuberculous diabetics. The difficulties encountered today are found chiefly in patients with advanced tuberculosis and hard-to-control diabetes.

An analysis of the findings in 70 patients in whom tuberculosis and diabetes were associated and who were followed for at least one year revealed many instructive facts relating to the interaction of the 2 diseases. The patients (32 men and 38 women) ranged in age from 30 to 70 years (average, 53). The diabetes preceded the tuberculosis in 42 patients, followed it in 11, and was diagnosed at the same time as the tuberculosis in 17. The general condition of the patients at hospitalization was good in 38, mediocre in 27, and poor in 4. Ten patients were febrile, 47 afebrile, and 13 subfebrile. Mycobacterium tuberculosis was present in the sputum of 51. The tuberculosis was advanced in 38%, and cavitary in 80%. Treatment of the tuberculosis consisted of rest and the administration of antituberculous drugs. Streptomycin, isoniazid, and aminosalicylic acid were used in various combinations, none of which produced any side-effects on the diabetes. The same treatment can, therefore, be used for tuberculous patients, both with and without diabetes, and the combined treatment of both diseases often makes it possible for diabetic patients to undergo thoracic operations safely.

The first consideration in treating the diabetes is to regularize the diet and the level of the blood sugar. The caloric value and the composition of the diet must meet the needs of the patient's tuberculous condition. The regimen adopted for the authors' patients provided 2,200 calories with the addition or subtraction of 200 calories as required. The basic diet is composed of 180 Gm. of carbohydrate, 90 Gm. of protein, and 130 Gm. of fat, apportioned according to the fluctuations of the blood sugar. Insulin was given as follows: (1) crystalline insulin in solution morning and evening to 27 patients; (2) protamine zinc insulin alone in the morning to 27; (3) a combination of crystalline insulin solution and protamine zinc to 4; (4) Invenol tablets, morning, noon, and evening, to 6; (5) a combination of Invenol and insulin to 1; and (6) no insulin to 5. The blood sugar was stabilized at 1-2 Gm. per 100 cc. in 33 patients and at 2-3 Gm. per 100 cc. in 29; but in the other 8 stabilization proved difficult. Investigations in recent years have established a connection between tuberculosis and the existence of a relative or absolute hypersecretion of the adrenals in diabetes. This hypersecretion, which is increased in hard-to-control diabetes, may exert an adverse influence on the course of the tuberculosis; consequently, control of the diabetes is of paramount importance when the 2 diseases coexist.

The results of treatment in these patients were satisfactory and not essentially different from those obtained in tuberculous patients without diabetes. The number of those in good condition increased from 56 to 80%; those without fever increased from 67 to 87%; and the sputum became negative in 67%, as compared with the original 27%. The percentage of improvement in patients with cavitary tuberculosis was 71%. Radiologically, 77% (54) of the patients showed improvement; 13% (9) were unchanged; and 4% (3) were worse. Only 4 patients (6%) died.

Use of Iproniazid Phosphate in Treatment of Angina Pectoris. C. Fauda and C. Candiani. Minerva med. 50:1924-1932 (June 13) 1959 (In Italian) [Turin, Italy].

Iproniazid phosphate was administered to 20 hospitalized and 60 outpatients, aged between 29 and 75 years, with angina pectoris related to a coronary disorder. The daily dose of the drug ranged from 100 to 150 mg. and was administered orally in 2 or 3 tablets. This dose was reduced later to about 75 mg. per day. There were 88 courses of treatment, each course lasting, on an average, 34 days, with drug-free periods of from 25 to 105 days in between. Marked improvement was obtained in 39 patients (48.7%) in the sense of a complete, or almost complete, disappearance of pain, or a considerable decrease in the amount of glyceryl trinitrate administered. Partial improvement resulted in 18 patients (22.5%), but there was no improvement in 23.

After the completion of therapy, electrocardiographic findings remained unchanged in 35 patients (43.8%), clearly improved in 19 (23.7%), and possibly improved in another 8. A comparative exertion test was made in 11 patients, and improvement was established in 8. The hypoxia test was given to 6 patients who demonstrated normalization of the cardiac function. A control test with placebos in 40 patients (50%) showed subjective improvement in 8 (20%). Iproniazid phosphate caused frequent mild or moderate, but not severe, side-effects in all except 2 patients, for whom administration of the drug was discontinued. The main side-effects consisted of urinary or neuropsychic disturbances, pain in the legs, body balance instability, tremor, sexual impotence, and hypotension. Iproniazid phosphate can thus be recommended for an effective management of angina pectoris. The lowest optimum dose level should be sought in order to prevent frequent side-effects related to the drug.

Arterial Insufflation of Oxygen in the Therapy of Peripheral Vascular Diseases. J. F. Visser. Nederl. tijdschr. geneesk. 103:1386-1388 (July 4) 1959 (In Dutch) [Amsterdam].

Visser points out that the therapeutic effect of intra-arterial insufflation of oxygen was discovered by Lemaire in 1948, when he tried to study vascular lesions with the aid of oxygen insufflation, and found that the complaints of patients who were examined in this manner were greatly reduced. After citing several observers who have reported on the therapeutic use of the method, the author describes his own experiences with it in 32 patients (4 women and 28 men). Two of the patients had thromboangiitis obliterans (Buerger's disease); all the others had arteriosclerosis obliterans. Gangrene existed in 8 of the patients. Sixteen patients complained of nocturnal pain or pain at rest. Three patients had diabetes mellitus.

The number of insufflations ranged from 4 to 9, the usual number being 6. The interval between injections was from 5 to 7 days. The average quantity of oxygen injected was 50 or 60 cc. In the presence of painful gangrene not more than from 10 to 20 cc. should be given at the first injection. The results obtained were good in 20 of the 30 patients with arteriosclerosis, and moderately good in 4; in 6 no effect was noticeable. One of the patients who failed to respond was a 74-year-old diabetic. In some patients long-standing, violent vascular pains in pregangrene were rapidly dispelled by this method. The effect may be the result of a nonspecific stimulation of the vascular walls.

The technique of the insufflation is simple. The oxygen is introduced slowly into the femoral artery with about the speed of an intravenous injection. The oxygen advances with the blood stream toward the periphery. In order to avoid its progression in the proximal direction, the patient is put in Trendelenburg's position, and the injection pressure should not be too high. The insufflation is followed by blanching of the member, as if an arterial embolism had developed. The skin temperature usually declines, but only for a few minutes, then irregular red, blue, and livid spots appear, which after about 10 minutes are replaced by a more uniform rose coloration. The patients generally complain only of a prickling sensation, which disappears in from 15 to 20 minutes. Complications, such as tonoclonic spasms, speech disturbances, or temporary hemipareses, are rare, and are due to technical errors. Caution is necessary in patients with coronary sclerosis, hypertension, or extensive varicosities.

Serum Transaminases in Hepatopathies: Importance of the Glutamic Oxalacetic/Glutamic Pyruvic Transaminase Ratio. A. L. B. Nery and P. O. Granato. Rev. brasil. med. 15:399-401 (June) 1959 (In Portuguese) [Rio de Janeiro].

The levels of serum glutamic oxalacetic transaminase (SGO-T) and serum glutamic pyruvic transaminase (SGP-T) increase during the course of hepatic disease, due mainly to necrosis of liver cells. The authors studied these level variations and the SGO-T/SGP-T ratio in a group of 30 normal subjects (physicians and students at the Faculty of Medicine, University of Brazil in Rio de Janeiro) and in a group of 74 patients suffering from different types of hepatic disease. There were 33 patients in the acute, and 14 in the convalescing phase of infectious hepatitis; 7 with chronic hepatitis; 9 with liver cirrhosis; and 11 with extrahepatic obstructive jaundice. The average SGO-T/SGP-T ratio was 1.12 in the normal subjects. In the group of patients with liver diseases, this value was 0.66 in the acute, and 0.77 in the convalescing phase of infectious hepatitis; 1.40 and 1.47, respectively, in chronic hepatitis and in extrahepatic jaundice; and 1.88 in hepatic cirrhosis. These determinations have a diagnostic value in acute infectious hepatitis, especially for its differentiation from extrahepatic jaundice. There is also a prognostic value as a criterion to estimate the course of infectious hepatitis. In this respect the SGO-T/SGP-T ratio is more significant than the absolute values. In chronic hepatic diseases the level of SGO-T remains high for a longer period than the level of SGP-T, which results in a ratio above the normal average.

Lupus Erythematosus Disseminatus: I. Analysis of a Clinical Material. J. Bichel, C. Holten and V. P. Petersen. Ugesk. laeger 121:933-941 (June 11) 1959 (In Danish) [Copenhagen].

Clinical, hematological, and serologic findings in 15 cases of disseminated lupus erythematosus are analyzed. The diagnosis, established on clinical signs and laboratory abnormalities, was verified in 14 cases by demonstration of the L. E. phenomenon and in 1 case by typical histological lesions found at autopsy. All the patients had joint symptoms, the commonest initial symptom in lupus erythematosus disseminatus, and in 13 there were fever periods, often of long duration. Skin symptoms were seen in 9 patients, 8 had heart disease, 11 had pleurisy and pneumonitis, and 8 had kidney disease. Neuropsychiatric disorders were found in 7 patients. Most of the patients had anemia and leukopenia. In 2 instances granulocytopenia with lymphocytosis had been present for 7 and 9 years respectively. False-positive seroreaction for syphilis occurred in 3 cases. Two patients seen in 1951-1954 have died. Thirteen patients given diagnoses since 1955 are in clinical remission; 5 are continuing treatment with a steroid; 3 are being treated with chloroquine; 5 are receiving no specific treatment. An additional 2 cases of the disease in women, aged 42 and 36 years, respectively, recently observed, are also described. The L. E. factor was demonstrated in both.

Diagnostic and Prognostic Value of the Pseudocholinesterase. M. Meeroff, J. Remolar and F. Muller. Rev. españ. enferm. ap. digest. 18:713-731 (May) 1959 (In Spanish) [Madrid].

The level of blood pseudocholinesterase (nonspecific cholinesterase which hydrolyzes also other choline esters besides acetylcholine) decreases in patients with liver damage. In 96 patients suffering from different types of hepatic disease, the plasma levels of pseudocholinesterase were determined by the Morand-Laborit technique, considering as normal values those between 40 and 50 units. Of the 20 patients in this series who had liver cirrhosis, 15 presented blood pseudocholinesterase values below 40 units; in 10 of them these values varied from 20 to 30 units, and in 3 they were below 20 units. In this group of cirrhotic patients the lowest levels always corresponded to serious clinical pictures, while the normal or near normal values corresponded to better anatomic and functional conditions of the liver—a correlation which was confirmed by other functional tests. In 10 patients with viral hepatitis the pseudocholinesterase values varied between 14.8 and 38.6 units, with the exception of a diabetic patient in whom the level was 56.2 units. Seven patients suffered from cardiac congestive liver; their blood pseudocholinesterase values varied from 18.6 to 38.1 units.

Similar values were determined in relation to other patients in the series who suffered from other types of hepatic disease, although normal or near normal values were found in 6 of the 9 patients with a choledochal syndrome of lithiasic origin. Comparing the pseudocholinesterase levels with other determinations, it was found that there was a parallelism between low pseudocholinesterase levels and hypoalbuminemia, especially in the cases of hepatic cirrhosis and viral hepatitis. Taking into consideration all the findings, it is suggested that the blood pseudocholinesterase level has a relative diagnostic significance and an undoubted prognostic value concerning hepatic functional conditions. Its determination should, therefore, become an integral element in habitual examination with hepatography.

Lethal Polyarteritis in Rheumatoid Arthritis. C. Holten, T. Lund and V. P. Petersen. Ugesk. laeger 121:944-947 (June 11) 1959 (In Danish) [Copenhagen].

In rheumatoid arthritis, exacerbations and remissions occur in varying number and duration, which cannot be foretold in the individual cases. A man, aged 49 years, with severe rheumatoid arthritis of many years' standing had been receiving relatively large doses of cortisone for 2½ years. Because of the slight therapeutic value of the steroid treatment, it was gradually discontinued, and a clinical syndrome, consisting of fever, loss of weight, pleurisy, pericarditis, renal disease, retinopathy, and extensive necroses in skin and subcutis, developed. Repeated examinations for L. E. factor in the blood and pleural exudate were negative. Necrotizing angiitis was established on biopsy of skin and muscle. The clinical and hematological findings showed features in common with polyarteritis nodosa and systemic lupus erythematosus. The patient's general condition steadily declined, and he died after 4½ months. At autopsy vascular lesions were found in skin, muscle, and kidneys. The glomeruli showed diffuse thickening of the basement membrane with degenerative changes in the tubules.

Gouty Arthritis: Current Concepts in Treatment and Control. J. H. Talbott. Minnesota Med. 42:1044-1052 (Aug.) 1959 [St. Paul].

The author reviews the data on 54 patients who were followed during the 1930's as well as those on 114 patients treated at the Buffalo Veterans Administration Hospital between 1948 and 1958. He reports on the diagnostic and therapeutic aspects of gouty arthritis. A presumptive diagnosis of acute gout should be entertained in any acute inflammation of one or more joints, particularly in a man. The clinical characteristic signs, such as inflammation, redness, swelling, heat, and tenderness, are among the most helpful diagnostic criteria. Although the concentration of serum uric acid is helpful, especially in confirming the diagnosis, the interpretation of this test should be done very carefully. A false normal value may be reported if the patient has received antiarthritic drugs within a 48-hour period prior to the collection of serum. Colchicine is the only specific antigout agent that has no recognized effect upon the uric acid metabolism; therefore, its administration needs not be stopped or withheld in view of the chemical analysis of serum uric acid.

The drug of choice in the acute attack of gout, whether the diagnosis has been confirmed or merely suspected, is colchicine. It should be administered orally without delay, 1 mg. every 2 hours until the onset of gastrointestinal reactions. It should then be replaced by a gastric sedative (tincture of paregoric). Colchicine may also be given intravenously in 2 or 3 doses, with a 3-hour interval between the injections. The response to the therapy may be valuable in confirming the diagnosis as well as in alleviating the joint discomfort. If colchicine is administered in less than the full amount, phenylbutazone in doses of 400 to 800 mg. daily may be added during 2 or 3 days. If an attack has been untreated, or treated insufficiently for one or more days, supplementary phenylbutazone or supplementary corticotropin (ACTH) is recommended. ACTH-gel should be given in doses of 60 to 80 units for 2 days. Prophylactic treatment between attacks includes the administration of colchicine combined with an uricosuric agent and the imposition of a balanced diet (avoiding foods with a high purine content). Probenecid is a powerful uricosuric agent with mild toxicity. Gastrointestinal distress from this drug may be prevented by its ingestion with a meal or the concomitant administration of a mild gastric sedative.

Deaths from Bites and Stings of Venomous Animals and Insects in the United States. H. M. Parrish. A. M. A. Arch. Int. Med. **104**:198-207 (Aug.) 1959 [Chicago].

The author analyzed the death certificates of all persons in the United States who died of bites and stings of venomous animals and insects during the 5-year period from 1950 through 1954. These certificates were supplied by the National Office of Vital Statistics, U. S. Public Health Service, Washington, D. C. There were 215 human deaths during the 5-year period, or an average of 43 deaths per year from this cause. This gives an average death rate of 0.28 per one million population per year. The hymenoptera (bees, wasps, hornets, yellow jackets, and ants) killed 86 (40%) of the 215 persons, poisonous snakes killed 71 (33%), and poisonous spiders killed 39 (18%). Other animals and insects causing fatalities were scorpions, sting rays, coelenterates, and unidentified venomous insects and animals. The rattlesnakes (Crotalus sp.) were the most dangerous venomous animals, accounting for 55 deaths, while the bees were the next most deadly, taking 52 human lives. Males were fatally bitten and stung about 2.6 times as often as females. The very young, 1 to 19 years of age, died of snake and spider venoms most frequently, whereas adults were the most frequent victims of stings by the hymenoptera. Usually several hours elapsed between the snake and spider bites and the victims' deaths. By way of contrast, 88% of the deaths from hymenopteran stings happened within one hour after the sting; these deaths were attributed to anaphylaxis resulting from allergy.

Deaths from venomous animals and insects were reported from 34 of the 48 states. The highest average death rates were found in the following states: Arizona, Georgia, Texas, Florida, Mississippi, Kentucky, Alabama, Arkansas, and Wyoming. Fatal bites and stings occurred more frequently during the warmer months of the year, from April through October. On the basis of this study it appears that previous estimates of the incidence of bites and stings by venomous animals and insects are far too low.

Correlation Between in Vitro Studies and Response to Antibiotic Therapy in Staphylococcic Bacteremia. F. M. Abboud and B. A. Waisbren. A. M. A. Arch. Int. Med. **104**:226-233 (Aug.) 1959 [Chicago].

In this study the reliability of the tube-dilution sensitivity test was investigated by a correlation of the result of the sensitivity in vitro by the tube-dilution method with the effect of the administration of various antibiotics to patients with staphylococcic bacteremia. Case records of 100 consecutive patients with bacteremia due to Staphylococcus pyogenes var. aureus, who were treated at the Milwaukee County Hospital in Wauwatosa, Wis., between 1952 and 1957, were studied. A heavy bacterial inoculum (1:100 dilution of an 18-hour culture, which is approximately 1,000,000) was added to the test dilution of the antibiotic. The minimal inhibitory concentration was determined by the absence of gross visual turbidity after incubation for 18 hours. The concentrations ranged from 100 to 0.38 mcg. per milliliter. Separate charts were then drawn for each antibiotic, with its minimal inhibitory concentration in micrograms per milliliter obtained in vitro plotted against the type of clinical response, determined in every case in which this antibiotic was administered.

The study revealed a definite correlation between the in vitro sensitivity of Staph. pyogenes var. aureus by the tube-dilution method to the various antibiotics and the clinical response obtained when these antibiotics were administered. The details regarding each antibiotic are discussed. In only one case did a clinical response occur when the in vitro results showed the organism to be resistant to 6 mcg. of an antibiotic per milliliter, but there was not always a clinical response when the organism was more sensitive. This suggests that the clinician should not give patients antibiotics to which the infecting staphylococci are resistant in vitro by the tube-dilution method. It further suggests that in vitro sensitivity tests by this method are no guarantee of clinical results and that host factors and complications must always be considered. The use of a single concentration of 6 mcg. of antibiotic per milliliter is suggested as a practical modification for the tube-dilution method of determining staphylococcic sensitivity to antibiotics. Massive dosages of penicillin did not effect a cure in a single instance when the staphylococci were resistant to a concentration of 6 mcg. of penicillin per milliliter in vitro. In a few cases staphylococci that were able to produce penicillinase were apparently eradicated by penicillin therapy.

Acute Tubular Necrosis: Analysis of One Hundred Cases with Respect to Mortality, Complications, and Treatment With and Without Dialysis.

L. W. Bluemle Jr., G. D. Webster Jr. and J. R. Elkinton. A. M. A. Arch. Int. Med. 104:180-197 (Aug.) 1959 [Chicago].

Acute tubular necrosis encompasses a variety of causes and degrees of parenchymatous damage and is frequently difficult to differentiate clinically or even pathologically from other types of acute renal failure. The 100 patients discussed were under the care of one or all of the authors between 1949 and 1958. The onset, course, or autopsy findings in these patients indicated that potentially reversible renal tubular necrosis was present. The authors omitted cases in which it appeared that the onset of diuresis was secondary to the correction of hypotension, hyponatremia, or dehydration rather than to healing of the tubular lesion, also cases of acute glomerulonephritis and acute pyelonephritis. They did not exclude, though, cases with preexistent renal disease if the clinicopathological picture indicated that acute tubular necrosis was superimposed, or cases in which oliguria lasted less than 4 days when the subsequent course or pathological examination revealed distinct evidence of renal damage. They also included 2 cases of bilateral cortical necrosis. Twenty-two patients were initially inpatients at the Hospital of the University of Pennsylvania in Philadelphia; 75 were transferred from other hospitals between the 2nd and 13th days of their disease (mean, 6.8 days); the remaining 3 were seen in nearby hospitals.

The over-all mortality rate was 50%, and the authors feel that this indicates that the efficacy of modern management has, at times, been overestimated and that the serious prognosis of acute tubular necrosis needs reemphasis. The mortality was related to the etiological background. There were 23 deaths among the 32 patients (72%) in the surgical group, but 11 of these deaths were probably due to the basic disease process present before renal damage occurred, such as abdominal infection, congestive heart failure in patients undergoing cardiac surgery, adrenal insufficiency, separation of abdominal aortic grafts, and myocardial infarction. Five of 6 patients with severe trauma died, but the renal lesion was thought to be directly responsible for death in 2 patients. Death in the others appeared to result from the initial injury. Of the 24 patients in whom the renal lesion developed after incompatible transfusion, 7 died, and of the 16 in whom the renal lesion was an obstetric complication, 4 died.

There was a high incidence of complications, and these contributed greatly to the mortality figures. Eighty per cent of all patients developed some evidence of infection, and this complication was primarily responsible for one-third of all deaths. Other common complications were potassium intoxication, cardiac arrhythmias, congestive failure, central nervous system disturbance, bleeding, and delayed wound healing. Certain aspects of therapy are reviewed. Hemodialysis was carried out in 52 cases. While it is difficult to evaluate the effect of this procedure on mortality statistics, the authors agree with others that it is a valuable therapeutic adjunct. Earlier and more frequent dialysis may decrease the incidence of complications. Further improvement in prognosis will depend upon more effective measures for preventing and treating the complications associated with acute tubular necrosis. This, in turn, will require a better understanding of the mechanisms by which the sudden loss of renal function predisposes to these complications.

The Alcohol-Intolerance Syndrome in Hodgkin's Disease.

J. Bichel. Acta med. scandinav. 164:105-112 (no. 2) 1959 (In English) [Stockholm].

The transient phenomenon of alcohol intolerance occurs more frequently in patients with Hodgkin's disease than in those with any other condition. It usually develops after an exacerbation of the disease and often disappears after a course of roentgenotherapy or chemotherapy, only to reappear during a relapse. In some patients, however, alcohol intolerance disappears after a successful treatment and does not recur during relapse; in others again, it may be present as the only subjective symptom for long periods. In a total of 116 patients with Hodgkin's disease, 25 exhibited alcohol intolerance on one or more occasions when seen in the Cancer Clinic of Aarhus, Denmark. The most frequent symptom of alcohol intolerance, and the one which causes the most discomfort, is pain, but it is rarely the only symptom which develops in the patient with Hodgkin's disease after alcohol ingestion. It may manifest itself in different ways, such as malaise, paresthesia, paresis, dyspnea, palpitation, pruritus, and various others. The alcohol-induced pain seems to be localized in, or radiating from, lymphogranulomatous tissue, affected lymph nodes, or, fairly often, infiltrated bones. In some patients of this series the enlargement of the affected lymph nodes was noticed immediately after ingestion of alcohol. This swelling causes particularly severe pain when the lymphogranulomatous tissue is encapsuled in bony structures. Sixteen of the patients with alcohol-induced pain had demonstrable destruction of bone, which was localized in the sternum in 7.

It is evident that alcohol-induced pain is not pathognomonic of Hodgkin's disease; nevertheless, its high occurrence in patients with this disease suggests that whenever the alcohol intolerance syndrome is present, the diagnosis of Hodgkin's disease should be considered. The mechanism of the alcohol intolerance syndrome is not known, but it may be that a study of this reaction will contribute toward elucidation of the pathogenesis of Hodgkin's disease.

SURGERY

The Effect of Hypophysectomy in Advanced Carcinoma of the Prostate. E. J. R. Smith, K. J. Gurling and D. N. Baron. Brit. J. Urol. 31:181-186 (June) 1959 [Edinburgh].

The authors report on 5 men, between the ages of 53 and 72 years, with advanced metastatic carcinoma of the prostate, who were subjected to surgical removal of the pituitary gland. One of the 5 patients died of left ventricular failure 72 hours after the operation. The 4 patients who survived the operation showed worth-while subjective and objective improvement. Regression of lymph node metastases and of the primary prostatic lesion was observed in all 4 survivors; it was usually apparent by the second week and was quite definite by the fourth week. Three of these patients had relapsed after responding to diethylstilbestrol-therapy preceding the hypophysectomy, but subsequently improved after hypophysectomy. Two of the 4 patients have lived for more than a year and have enjoyed a worth-while prolongation of life, and a third patient continues to do well 4 months after the operation. Pituitary ablation appears to be an effective means of palliating the late stages of carcinoma of the prostate, but until the indications and long-term effects are more clearly defined, it should remain primarily an investigational procedure.

Mesotheliomas of the Pleura. M. W. Wolcott, W. A. Shaver, H. E. Walkup and E. D. Peasley. Dis. Chest 36:119-126 (Aug.) 1959 [Chicago].

The authors report on 8 men, ranging in age from 24 to 59 years, who were treated at the Veterans Administration Hospital in Augusta, Ga., between 1948 and 1956 for tumors of the pleura, all of them of mesothelial origin. The neoplasms were diffuse in 6 patients and were solitary in 2; the tumor was malignant in one of the latter patients. The finding of massive pleural effusion associated with nodulations on the thoracic wall or on the surface of the lung parenchyma is believed to be suggestive of the diffuse type of tumor; bloody effusion was characteristic in each of the 6 patients with diffuse mesotheliomas. The rapid onset of symptoms observed in 4 of the 6 patients is believed to be of some diagnostic value. The longest duration of symptoms prior to hospitalization was 3 months. There was a history of spontaneous pneumothorax in 2 patients, which occurred on the same side as the tumor. Dyspnea and chest pain of the pleuritic type were present in all 6 patients with diffuse mesotheliomas. It is believed that the diagnosis of diffuse mesothelioma must be differentiated from metastatic carcinoma, which is done by exclusion of all possible primary sites.

The solitary mesotheliomas in the 2 patients arose from visceral pleural surfaces. They did not show any effusion. The lesion had been present in one patient for 5 months and in the other for at least 2 years prior to surgery. Neither of the 2 patients had symptoms of arthralgia or chest pain, nor were there any findings of pulmonary arthropathy. Roentgenologic findings showed a solitary, well-circumscribed tumor without satellite nodules. All the patients with diffuse mesotheliomas died within 2 to 40 months from the onset of symptoms. Neither surgery nor roentgen-ray treatment had been of any value. Excisional therapy which had been performed in the 2 patients with solitary mesotheliomas showed good results. Both of these patients were living 1 year and 4 years, respectively, after surgery, and they did not show any evidence of recurrence.

Brachyesophagus: Pathogenesis, Diagnosis and Clinical Course of Congenital and Acquired Short Esophagus. R. M. Konrad and F. Rotthoff. Beitr. klin. Chir. 198:448-462 (no. 4) 1959 (In German) [Munich, Germany].

The authors report on 5 patients with congenital short esophagus with the stomach herniated into the thorax (group 1) and 6 patients with secondary, acquired short esophagus with hiatus hernia of sliding type (group 2), who were observed among 100 patients admitted for hiatus hernia to the surgical clinic of the Medical Academy in Düsseldorf, Germany. Group 1 consisted of 2 male infants, aged 1 year and 9 months, 2 female infants, aged 6 months and 2 years, and a 36-year-old woman. Group 2 consisted of 2 men, aged 37 and 55 years, and 4 women, between the ages of 56 and 61 years. The clinical manifestations of the infants in group 1 were quite similar, including inadequate sucking effort, postprandial vomiting, a high degree of anemia, and massive hemorrhages in the form of melena and hematemesis. The roentgenologic examination revealed the typical signs of short esophagus, i. e., the esophagus extending to the 7th and 8th thoracic vertebrae, and the intrathoracic portion of the stomach showing a tubular shape. A transthoracic approach was employed for the surgical intervention in group 1; the esophagus was mobilized, the intrathoracic portion of the stomach was replaced subdiaphragmatically, and the esophagus was fixed in the hiatus-slit. In one of the patients reposition of the stomach was impossible because of the short esophagus, and, therefore, only the stenosis was corrected. Recurrences occurred in 2 of the children and in the adult. The latter patient was subjected to reoperation twice; then a normal anatomic situation was revealed on roentgenologic examination.

In the patients of group 2 a primary reflux-esophagitis associated with incontinence of the cardia was the cause of the secondarily shrunken, acquired short esophagus. All 6 patients had dysphagia and postprandial complaints, such as belching, heartburn, nausea, and vomiting. Signs of shortening of the esophagus were observed in the roentgenograms of all 6 patients, with the orifice of the esophagus at the cardial pole of the stomach, and the stomach drawn into the thorax with the patient in the standing position. All the patients were operated on by means of the transthoracic approach, with the aid of intubation-curare anesthesia. A more or less markedly shortened esophagus made reposition of the stomach difficult in all the patients. In 2 patients who had been operated on recently, it was still too early for an evaluation of the postoperative results. One patient died of circulatory collapse on the second postoperative day. Normal conditions without reflux were restored in one patient. In one patient the motility in the lower portion of the esophagus was disturbed postoperatively, and the cardia was gaping with reflux; in another patient reflux was observed in the recumbent position with the head lowered.

The congenital type of short esophagus is caused by an arrest of development in the early embryonic stage. With the secondary type, apparent and real shortening of the esophagus has to be distinguished. The apparently shortened esophagus is due to a contraction of the longitudinal muscles, while the real shortening is attributed to a cicatrized longitudinal shrinking of the wall of the esophagus, which occurs mostly as a result of primary reflux-esophagitis. Both the congenital and the acquired types of the disease are rare. The treatment is surgical, but reduction of the herniated stomach may be impossible when there is a high degree of shortening of the esophagus. The reported operative results cannot yet be considered as a fully satisfactory solution.

Treatment by Hemispherectomy of Nine Cases of Spastic Hemiplegia, Severe Mental Retardation and Intractable Epilepsy. A. Morello, F. J. O'Neill and T. L. Hoen. Psychiat. Quart. 33:44-54 (no. 1) 1959 [Utica, N. Y.].

The authors performed hemispherectomy on 9 patients with spastic hemiplegia, severe mental retardation, and intractable epilepsy at the Central Islip (N. Y.) State Hospital. The intervention consisted of the removal of one entire cerebral hemisphere through a large fronto-temporo-parieto-occipital bone flap, with the aid of general anesthesia. The postoperative course was smooth in some of these patients, stormy in others. However, the facts that each patient withstood the procedure well and that the patients reacted quickly after the intervention were impressive. The patients were given sedatives to combat agitation and excessive motor activity. Every patient regained consciousness within 2 hours after the operation. There was only one death. Clinical observations of one patient, a 10-year-old boy, included 2 most impressive facts: The muscular spasticity diminished markedly; no epileptic seizures occurred. As a result of the lessened spasticity, the patient's arm and hand postures have greatly improved, and wider movements are possible. Although the follow-up period is still short, it would seem justified to classify the result as excellent. In the other 8 patients, the results were, on the average, satisfactory.

Interatrial Septal Defect with Associated Transposition of the Pulmonary Veins: Surgical Treatment. G. Rotthoff, L. Lojacono, V. Puchetti and A. R. Fahmy. Chir. ital. 11:249-269 (June) 1959 (In Italian) [Milan, Italy].

The authors found a transposition of the pulmonary veins in 44 patients among 235 with interatrial septal defects. The veins of the right superior lobe were transposed in 40 instances. The transposed veins were connected with the right atrium in 33 instances and with the vena cava superior in 18. Electrocardiography was an important diagnostic aid; it also helped to distinguish "ostium primum" from "foramen secundum." The purpose of the operation was to correct simultaneously, if possible, both the interatrial septal defect and the abnormality of the pulmonary veins.

Full success in correcting transposed pulmonary veins terminating in the wall of the right atrium was obtained in 9 instances. Of 18 patients with transposition of the pulmonary veins terminating in the vena cava superior, full correction was obtained in 3. There seemed to be no greater incidence of operative complications in patients operated on for both abnormalities than for the interatrial septal defect alone. Ventricular fibrillation, which developed in one patient, was resolved by electroshock and heart massage; postoperative cyanosis developed in 3 patients; interatrial communication persisted in 3 patients after the operation; and a left-right shunt, exceeding slightly 1 liter, was observed in 2 more patients. Death occurred in only 5 patients of the series of 44. The authors suggest that surgical correction of the interatrial septal defect with associated transposition of the pulmonary veins be made early in life, but not below the age of 4 years.

Problems in Diagnosis and Treatment of Hyperparathyroidism. G. J. Renes. Arch. chir. neerl. 11:179-192 (no. 2) 1959 (In English) [Arnhem, Netherlands].

The author reports on a 52-year-old man with combined osseous and renal hyperparathyroidism, who was admitted to the Bethesda Hospital in Djokjakarta, Indonesia, for a fracture of the right femur with multiple cystic degeneration of the bone. An excessive amount of calcium was determined in the patient's blood on repeated examinations. The serum phosphorus level was normal. Hypercalciuria was investigated only once and was not observed. The serum alkaline phosphatase level was not studied, but despite the incomplete biochemical aspect, the diagnosis of hyperparathyroidism was made because of the typical generalized cystic osteitis. The patient had a constant albuminuria; urinalysis revealed leukocytes and erythrocytes. An abdominal scout roentgenogram showed extensive nephrolithiasis. The intravenous pyelogram revealed much impaired function of the right kidney.

The patient was operated on, and the usual low transverse cervical incision revealed a normal thyroid gland, except for a small, firm, round nodule which could be palpated in the left superior lobe. Ligation and cutting of a few lateral veins allowed the thyroid gland to be lifted out of its bed and rotated medially. This maneuver revealed atrophic, pale yellowish parathyroid glands. Following the left inferior thyroid artery, a deep-seated tumor was found lying between the arterial ramifications. The tumor could be shelled out easily, preserving the artery. The operation was concluded by resecting the left superior thyroid lobe, carefully preserving the left superior parathyroid gland. Pathological examination of the operative specimens revealed a papilliferous cystadenoma in the left superior thyroid lobe. The parathyroid tumor consisted of several parts with intervening septums which were continuous with the capsule. Microscopically, the tumor showed numerous water-clear cells arranged in many small nests, and separated by a stroma which consisted of collagenous and hyaline connective tissue. The patient was placed on a calcium regimen; 1 Gm. of calcium was first given intravenously 3 times daily, and from the 10th postoperative day onward, 4.5 Gm. of calcium was given daily by mouth, with cod liver oil additionally. One month after the operation the calcium serum levels were still low, ranging from 7.7 to 9 mg. per 100 cc. Fracture healing, which had been very much delayed, progressed rapidly after removal of the parathyroid adenoma. One month after the operation, a right ureteral stone was removed surgically. At the end of this operation paroxysmal tachycardia occurred, which was stopped abruptly by an intravenous injection of 1 Gm. of calcium chloride. As the patient had received 1 Gm. of calcium chloride prophylactically one hour before the operation, this occurrence was rather unexpected. The serum calcium level determined shortly after the second calcium administration was only 7.1 mg. per 100 cc.

Hyperparathyroidism gives rise to an extremely variable clinical picture. Osseous changes are often not discernible. Conditions of osseous and abdominal hyperparathyroidism are cured after removal of the hyperfunctioning parathyroid tissue, but renal changes soon become irreversible. Early diagnosis is most important. Postoperative tetany should be prevented. When further operations, i. e., removal of urinary stones, are deemed necessary, it should be appreciated that, after removal of the adenomatous or hyperplastic parathyroid glands, calcium metabolism is unstable for several months, and prophylactic measures should be taken accordingly.

The Importance of Early Diagnosis of Bronchogenic Carcinoma: Clinical Analysis of 236 Cases of Bronchogenic Cancer in the Municipality of Shanghai. M. H. Shih, S. Y. Ku and C. P. Chang. Chinese M. J. 79:19-25 (July) 1959 [Peking].

The authors report on 236 patients (183 men and 53 women) with bronchogenic carcinoma, who were seen in 16 different hospitals in Shanghai between 1949 and 1957. Of the 236 patients, 197 were older than 40 years. Roentgenologic, bronchoscopic, and cytological examinations are the 3 important means for the diagnosis of early stage bronchogenic carcinoma. In this series, the roentgenologic examination showed tumor shadows in all the patients. Bronchoscopy, performed on 163 patients, yielded positive results in 103. Exfoliative cytological examinations were performed in 113 cases and revealed cancer cells in only 32. Biopsy is helpful in determining the type of lung cancer, and suitable radiotherapy or antitumor antibiotic therapy may be considered. The diagnosis in this series was made by bronchoscopic biopsy in 42 patients, by sputum examination in 32, by lymph-node biopsy in 80, by liver biopsy in 2, and by examination of the biopsy specimen obtained from pneumonectomy in 125. Diagnosis was established in 2 patients by examination of the tissue coughed up, and in 8 patients at autopsy. Eight patients had squamous-cell carcinoma, 62 had adenocarcinoma, 41 had undifferentiated carcinoma, and 53 unclassified types.

The results of treatment in the 236 patients with bronchogenic carcinoma were far from satisfactory. This was due partly to a delay on the part of the patients in seeking treatment and partly to the establishment of a false diagnosis on the part of the clinicians. Both factors were responsible for the fact that at the time of admission the patients already had far-reaching and extensive metastases. Ninety-six patients were considered inoperable. Eight patients, whose disease was operable, refused to be operated on. Exploratory thoracotomy was carried out in 61 patients, all of whom were found to be inoperable. Of the entire series, only 71 patients were operable, and of these, only one-half could undergo a radical resection. Nine of these patients died after the operation, the operative mortality being 12.7%. Of the 62 patients who were discharged after the operation, 8 were lost to follow-up. Of the remaining 54 patients, only 7 survived for more than one year without metastasis or recurrence after the operation. Two of these 7 patients had survived almost 4 years when the study was completed. The resectability rate in this series was low, and more than half of the resections were of the palliative nature; in 65% metastases to the mediastinal lymph nodes were present. The poor therapeutic results are closely related to the late diagnosis.

Localized Mesotheliomas of the Pleura. C. Kerrinnes and A. Gläser. Beitr. klin. Chir. 198:377-389 (no. 4) 1959 (In German) [Munich, Germany].

The authors report on 2 men, aged 51 and 52 years, a 56-year-old woman, and a 11½-year-old girl with localized mesotheliomas of the pleura, who were operated on in the department of pulmonary surgery of the surgical University Clinic in Leipzig, Germany. The site, form, and size of these benign tumors of the pleura varied considerably in the 4 patients: The tumors were situated in the area of the right apex in 2 patients; a tumor the size of a chestnut with a long pedicle was found at the lobar fissure in one patient; and one patient showed marked signs of displacement of the mediastinum, dyspnea, and the osteoarticular symptoms reported by Clagett and his associates. The maximum weight of the tumors amounted to 2.4 kg. (5½ lb.). The generally benign localized variants cannot always strictly be separated from the malignant diffuse ones, and early radical surgical removal is, therefore, required also for the purely expansive, slowly growing localized tumors. In the presence of a giant tumor, the excision may be difficult, owing to increased vascularization causing diffuse hemorrhage of the thoracic wall. All 4 patients are now alive and have not had recurrences.

The structures of the tumors, observed on microscopic examination of the surgical specimens, suggested that all mesotheliomas may be derived from the surface cells. The capacity for differentiation of the mesotheliomas is reflected in the forms of the tumors; these have a partly pure mesenchymal, partly a predominantly epithelioid character, or they show the structure of an endothelioma. Giant cells were present in one of the tumors, and their presence in mesenchymal tumors of the pleura has also been reported by other workers. Degenerative changes, such as calcium deposits, hyaline swelling of the connective tissue, and necrosis, were observed in most of the specimens.

Esophagoscopy During Active Upper Gastrointestinal Hemorrhage. H. W. Smith. Connecticut M. J. 23:519-522 (Aug.) 1959 [New Haven].

The author performed esophagoscopy on 75 patients with upper gastrointestinal hemorrhage during the period of active bleeding. No complications were observed to arise from the examination. In no instance was it found necessary to abandon the procedure, and in all instances the true status of the esophagus was determined. Localization of the source of bleeding beyond the confines of the esophagus has not been considered in this paper.

It is emphasized that esophagoscopy in the presence of esophageal varices is not hazardous if reasonable care is used, but this procedure in the presence of actively bleeding varices is not for the occasional endoscopist. The examination should be performed with the patient under topical anesthesia with a minimum of sedation. The patient should be kept sufficiently active so as to continue his bleeding during the period of examination. Moreover, the operating table to which he should be adequately secured should be one which cannot be moved about by his movements and yet it should allow for rapid and variable positioning. An attempt should be made to obtain the patient's cooperation, the anticipated degree of which can easily be evaluated while placing the topical anesthesia. In most instances the insertion of the esophagoscope through the cricopharyngeal sphincter determines the ease with which the patient is managed from that point on. Massive hematemesis with the esophagoscope in position can be fatal, and this may be avoided by emptying the stomach when indicated. Observations are most reliably made on deep inspiration, for the walls of the esophagus are then at rest and the lumen widest. The cardiac sphincter is best observed when the esophagoscope is withdrawn from the stomach; this can be repeated with the patient in various positions to shift the flow of blood away from the area being examined. Rapid heaving respirations make the examination difficult, and in such instances the wall of the esophagus needs to be stabilized on the nonbevel side of the esophagoscope, allowing the mucosal surface to roll across the tip.

A patient with a clinical diagnosis of cirrhosis of the liver, presenting with a bleeding gastric or duodenal ulcer, should not be assumed to have varices and treated accordingly. Perhaps the patient with upper gastrointestinal hemorrhage of nonesophageal origin, presenting with border-line liver function studies, may be the one most helped by the vigorous diagnostic approach. A false diagnosis of bleeding esophageal varices established by presumption will thus be avoided, and the patient will be managed with the benefit of reliable information obtained by esophagoscopy.

Portacaval Anastomosis in Portal Hypertension. R. Trias Rubies. Med. clín. 32:168-172 (March) 1959 (In Spanish) [Barcelona].

A 40-year-old man was hospitalized with complaints of recurrent gastrointestinal disorders and attacks of blood vomiting and blood in the stools. The disease had lasted for about one year. The patient had lost weight and had moderate jaundice and painful hepatosplenomegaly. Liver tests were positive for insufficiency. Large-sized esophageal varices were seen on roentgenographic examination. The aspect of the liver on laparoscopy was that of nodular cirrhosis. Splenoportography and splenomanometry gave the clue for a diagnosis of portal hypertension. The lumen of the portal vein was dilated, the splenic vein was sinuous, and the elimination of the contrast medium during splenoportography was greatly delayed. The manometric tension reached figures as high as 25 cc. of water. In the course of the operation the liver proved to be cirrhotic and hypertensive. There was a large number of enlarged lymph nodes at the hilus of the liver. The operation consisted of the establishment of a shunt through an end-to-side portacaval anastomosis. Biopsies of the liver and of the hilar-lymph node showed nodular cirrhosis and chronic inflammation respectively. The postoperative period was uneventful.

One month later the esophageal varices and hepatosplenomegaly had disappeared. Liver functions had greatly improved, the improvement continuing up to the present date, 4 months after the operation. The author believes that portal hypertension is the cause of the formation of esophageal varices and of the severe hemorrhages of these varices. Its presence constitutes an indication for the establishment of a portacaval shunt. Portal hypertension in nodular cirrhosis of the liver is due to intrahepatic blockage of the portal vein. The cirrhotic nodules compress the parenchyma and the sinusoids of the liver, thus preventing portal blood inflow and favoring the development and bleeding of esophageal varices.

Local Fibrinolysis and Postoperative Hemorrhage in Thoracic Surgery. A. Dumont and L. De Geeter. Acta chir. belg. 58:335-345 (April) 1959 (In French) [Brussels].

The authors' studies of blood specimens, obtained from a patient with severe hemorrhage who died after a right upper lobectomy, have for the first time demonstrated the existence of a local fibrinolytic process in the thorax. This local fibrinolysis is apparently responsible for the diffuse, sometimes catastrophic hemorrhages that may occur immediately after endothoracic operations. The fluid thoracic blood that is obtained from the thoracic cavity or that escapes from a drain possesses all the characteristics of serum. This means that clotting took place normally but that the clots were later lysed by a lytic ferment produced on the spot.

The hematological findings showed that the plasma of the blood in the thoracic cavity contained a proteolytic agent capable of digesting casein and probably also fibrinogen and fibrin (plasmin has the power to digest these 3 proteins). No fibrinolytic process, on the other hand, was observable in the peripheral venous blood, which indicates that the fibrinolysis was a purely local phenomenon. It sometimes takes place with extreme rapidity, but it can be modified in loco by the local injection of massive doses of certain clotting agents (thrombin) or by the intravenous injection of fibrinogen or by the intrathoracic injection of an inhibitor of lysis, such as soybean extract (purified crystalline soybean tripsin inhibitor). Each of these procedures has been followed by an arrest of the hemorrhage; in some cases, the arrest was very abrupt and led to a dangerous accumulation of clots in the thorax. Each of the 3 should be considered worthy of trial in patients with massive hemorrhage after thoracic surgery, but the possibility that excessive clot formation in the thorax after an abrupt cessation of hemorrhage may necessitate a second operation to remove the clots should be kept in mind.

Right Hemicolectomy in the Treatment of Chronic Regional Enteritis. F. Loyudice, D. Mancini and F. Corrao. Prensa méd. argent. 46:275-284 (Jan. 30) 1959 (In Spanish) [Buenos Aires].

The records of 15 patients with chronic regional ileitis, who had had an operation during the years between 1947 and 1957 in the Instituto de Patologia Quirurgica of the University of Rome, were reviewed in 1958 for assessment of late results. At the time of operation the patients were young adults of either sex (with the exception of a 3-year-old boy and a 73-year-old man). They had been followed up for periods of 2 to 11 years. The patients had originally complained of chronic intestinal disorders of long duration; crises of acute abdominal pain, nausea, vomiting, and diarrhea were frequent, lasting for 2 or 3 weeks and recurring within 3 or 4 months. The patients had anemia and loss of weight. They all were hospitalized with acute symptoms of intestinal obstruction or partial obstruction and underwent emergency surgery, which consisted of a resection of the stenotic ileal segment, hemicolectomy, and ileotransversostomy in 12 cases and of other operations in 3 cases. The resected ileal segments showed the typical features of hypertrophic-granulomatous and sclerotic-ulcerative forms of chronic regional ileitis. The first form was observed in patients in whom the disease had lasted for several months; the lesions were limited to the terminal segment of the ileum in an extension of not more than 15 cm. Stenosis was due to inflammation of the intestinal wall. The second form was observed in patients in whom the disease had lasted for several years, and the lesions were severe. There was endarteritis of the mesenteric vessels. Stenosis was due to sclerotic narrowing of the intestinal wall. These 2 observed forms are successive stages of chronic regional ileitis.

Of the 12 patients who had resection and hemicolectomy, 8 (75%) recovered. The satisfactory results had remained permanent from 2 to 8 years after the operation. In the other 4 patients, the symptoms of intestinal stenosis were permanently controlled, but mild crises of abdominal pain and diarrhea still occurred. Of the 3 patients who did not have hemicolectomy, one died of a cardiovascular disease shortly after the substitute operation. Two patients had a simple resection; one was greatly improved, and the other recovered and was in normal health 11 years after the operation.

Osteochondritic Changes in the Head of the Femur after Reduction of Congenital Dislocation of the Hip. J. H. Kite. South. M. J. 52:945-951 (Aug.) 1959 [Birmingham, Ala.].

The author investigated the cause of osteochondritic changes in the femoral head after the reduction of congenital dislocation of the hip in 97 children. The ages of the patients ranged from less than 1 year to 5 years. Only to those cases in which there was a well-formed head before reduction, which degenerated and later regenerated, has the term "osteochondritis" been applied. Of the 97 patients, reduction was performed in 65 without traction; of these, 11 developed osteochondritis. Of the remaining 32 patients, in whom reduction was performed after they had been held in traction for from 3 to 5 weeks, 7 developed osteochondritis of the femoral head. Thus, osteochondritis occurred as frequently in those patients who had traction as in those in whom reduction was performed without traction. The 18 patients, in whom osteochondritis occurred, were followed up for from 2 to 24 years, with an average of 7½ years. Eleven of them developed a thin femoral head with a smooth outline, giving a fair functional result. Five patients presented a rather severe coxa vara. Two patients developed a mushroom-shaped head too large for the acetabulum. When followed up into adult life, they all had very short femoral necks. In one patient the head disappeared completely and had not reappeared 4 years after reduction.

It is believed that osteochondritis is probably due to the atrophy which develops after complete immobilization of the hip in cast. It does not seem to be the pressure of the head of the femur against the acetabulum that causes osteochondritis, but the reverse, the lack of pressure. It is suggested that traction be used only in those cases in which reduction is difficult.

Low Back Pain Due to Arterial Obstruction. D. L. Filtzer and H. T. Bahnson. J. Bone & Joint Surg. 41B:244-247 (May) 1959 [London].

Of 60 patients with aortoiliac obstruction, seen by the authors at the Johns Hopkins Hospital between 1952 and 1958, 13 appeared with low back pain as the initial symptom. The diagnosis of aortoiliac obstruction was proved in each patient by either aortogram, surgical intervention, or both. In 2 of the 13 patients the low back pain was attributed to a previous injury to the back, and in one other patient to a urinary tract infection. Ten patients had been treated for neuromuscular disease of the back; in one of these, a ruptured intervertebral disk had been removed with relief of symptoms 8 years before the vascular symptoms occurred. In the others, the orthopedic treatment was not so clearly indicated, if at all. Four of the 13 patients with low back pain underwent lumbar sympathectomy with some relief of back pain, and another died after an extensive endarterectomy of the entire abdominal aorta. This left 8 patients available for follow-up study, who had had their circulation reestablished by endarterectomy or some type of arterial graft. Six (75%) of these 8 patients had relief of their low back symptoms after reestablishment of the circulation. In 2 patients no relief of back pain was obtained from the operation. One of these patients had clinical and roentgenologic evidence of degenerative disease originating in the disk, for which he had had previous nonoperative treatment.

A considerable proportion of patients with thrombosis of the aorta or its bifurcations have low back pain, either alone or in conjunction with other symptoms of this disease. Arterial obstruction should be considered in every patient presenting himself with low back pain. The importance of the history in making this diagnosis cannot be over-

NEUROLOGY & PSYCHIATRY

Treatment of Depressive States with Iproniazid. A. Tellez, M. Estay and Juan Brzovic. Rev. méd. Chile 87:430-438 (June) 1959 (In Spanish) [Santiago].

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Iproniazid was administered orally in tablets of 50 mg. The daily dose varied from 50 to 300 mg. over 8 to 12 hours. The average total dose varied between 7,727 mg. in the reactional depression group and 12,388 mg. in the mixed depression group. The average daily dose was 112 mg. during the period of intensive therapy, and approximately 50 mg. during the maintenance stage. The highest individual daily doses were 300 mg. for 2 patients with schizophrenia and 250 mg. for 2 patients with elements of phobia and obsession. The highest individual total doses were 20,175 mg. for a patient with mixed depression and obsession, who was cured; 18,200 mg. for a patient with schizophrenia, who did not experience satisfactory improvement; and 18,000 for a patient with endogenous depression, who obtained satisfactory but temporary improvement. Although there were frequent side effects, the medication had to be suspended in only a few exceptional cases. The most serious reactions were hypotension, urinary disorders, changes in sexual activity, and constipation.

The results of the iproniazid treatment were evaluated as satisfactory, or radical, and unsatisfactory, or slight. They were also analyzed from 3 viewpoints: 1. Over-all results in relation to the general depressive state. There was improvement in 49 (90.6%) of the 54 patients treated. In 40 of them (74%), the improvement was satisfactory; and in 31 (63%), it persisted after the 3 months of more intensive therapy. 2. Results in the different groups. Satisfactory results were obtained in all 16 patients in the reactional depression group, in 5 of the 6 patients with involutional depression, in 8 of the 11 with mixed depression, in 4 of the 6 with organic mental disorder, and in 8 of the 15 with endogenous depression (including schizophrenia, mania, epilepsy, etc.) In the groups with organic and mixed depression, there was a relapse in 80 and 54.6%, respectively, of the patients who experienced satisfactory improvement. 3. Results in relation to specific symptoms. Anxiety was the symptom which improved in the largest percentage of patients (96.2%); the lowest percentage of improvement (85.4%) was observed in relation to somber prospects concerning the future. The improvement was more stable in relation to anxiety, sadness, and depressive ideas, whereas there were frequent relapses in relation to pessimism and loss of social interest. The over-all results indicated that iproniazid was more effective in reactional and involutional depressions than it was in the depressive states which included organic and/or endogenous elements.

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In the series reported here, 130 patients suffered from functional disabilities of the upper limbs. Their rehabilitation was evaluated according to a 0-100 percentage scale, in which 0 represented persistence of the disability; 25% represented functional recuperation of a small part of the limb involved; 50% corresponded to recuperation of some functions with persistence of serious impairment of others; 75% represented normal function of the limb, except for certain efforts; and 100% meant complete normalization. In this group the gains amounted to 25% of 43 patients, 50% in 51, 75% in 20, and 100% in 7. The other patients (807) suffered from postpoliomyelitis disabilities of the lower limbs. For this group the 0-100 percentage scale of improvement had the following values: 0 corresponded to persistence of the disability;

emphasized. Back or leg pain or both, coming on after exertion, should suggest the diagnosis even in the absence of the other well-recognized symptoms of arterial insufficiency. Therefore, to affirm or deny this suspicion, it is essential that palpation of the femoral and peripheral pulses be made a routine and integral part of every orthopedic examination in patients complaining of low back pain. When pulses are not palpable or are diminished, and in the absence of other clear musculoskeletal disease, consideration should be given to further and more specific diagnostic procedures, such as aortography. Only in this way can an occasional baffling and elusive case of troublesome backache be fully understood and the appropriate treatment instituted.

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It is the consensus that no single factor is responsible for the unexpected bleeding which may complicate the clinical picture. The possibility of blood incompatibilities must be considered in the genesis of the oozing. Although no erythrocyte type specific incompatibility was seen in the 6 patients in this series, the icteric serum observed in 3 of them suggested excessive intravascular hemolysis. Thus, blood replacement is not considered to be the sole cause of the hemorrhagic complication. It is suggested that the basic disease or the nature of the surgical procedure is of major importance in the pathogenesis of the oozing.

If oozing develops and is thought to be associated with the transfused blood, it seems advisable to limit additional blood to that which is reasonably fresh and which has been collected in nonwettable containers. Specific defects should be treated when these are recognized. Human albumin solution may be of considerable help as plasma expander if used with other appropriate measures.

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The authors report the occurrence of bilateral congenital popliteal webbing in a female infant, the first child of normal parents, and in her brother, born one year later. The girl had a cleft of the soft palate and 2 congenital sinuses of the mucous membrane of the lower lip. She had skin webs extending from the region of the ischial tuberosities to the heels, the knees being held flexed 100 degrees. The toes were maldeveloped; only 3 toes were present on each foot, one being a true hallux and one a syndactyl of 2 digits; 4 metatarsals were present. In the boy, the same deformities in the mouth, legs, and feet were present as were present in his sister, except that the left foot had one hallux and 2 pairs of syndactylous toes, and the right foot had one hallux and no other toes.

Both infants were operated on, and the skin web of the popliteal fossa, extending from the ischial tuberosity to the heel, was adjusted by Z-plasty extending from the limits of the webbing, with excision of the fibrous web cord alone. The girl underwent operation on the right leg when she was 2 weeks old, and on the left leg at the age of 4 months. The boy was operated on between the 4th and 6th months of life. The gain in passive knee extension on the operation table was only about 30 degrees from the initial 100-degree contracture in both infants, but a steady improvement was obtained in the range with simple stretching and physical therapy. At the age of 2 years, the girl was able to stand unaided; active and passive extension of the knees was within 20 degrees of normal. At the age of 15 months, the boy's passive extension was 45 degrees from full, and was still increasing in both knees. There was no paralysis, and it became plain that the nerves can accommodate themselves to the gradual corrective extension of the knees. There was no evidence of weakness in the muscles supplied by the sciatic nerve. The maternal grandfather of the patients had a harelip, but there was no familial history of webbing.

The results obtained in these patients show that, although the sciatic nerve is unfavorably placed in the web, correction of the flexion deformity can apparently be carried out safely after plastic repair of the skin by Z-plasty and excision of the fibrous web cord alone, without causing a traction paralysis. The cases of these 2 patients appeared to be unique in that they were siblings of different sex with identical congenital abnormalities of bilateral webbing, cleft palate, and fistulas of the mucous membrane of the lower lip.

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25% represented walking with crutches and apparatuses; 50%, walking with either crutches or apparatuses; 75%, difficult walking without crutches or apparatuses; and 100%, normal walking. The gains amounted to 25% in 123 patients, 50% in 436, 75% in 165, and 100% in 72.

Specific improvements were observed among these patients in muscular tonus, increase in muscular temperature and thickness, longitudinal growth, recuperation or improvement of reflexes, improvements in muscular movements and physical capacity, and response to faradic or galvanic currents. The time necessary for reaching maximal results varied between 4 to 6 months and several years, according to the number and size of the muscles involved and the degree of disability. Small muscles responded better than large muscles to the treatment. The author is now using a combination of growth hormone, trophic substances, and vitamins, which he believes brings better results in a shorter time.

Experimental Focal Epilepsy in Animals. F. Morrell. A. M. A. Arch. Neurol. 1:141-147 (Aug.) 1959 [Chicago].

Investigators dealing with problems of the pathogenesis and pathophysiology of convulsive disorders have been concerned with discovering an animal preparation which, with reasonable fidelity, can mimic the chronic, recurrent, and paroxysmal disturbance of human epilepsy. The discovery of the aluminum hydroxide technique was a fundamental advance in this regard. Local injection or application of alumina (aluminum oxide) cream will produce a chronically discharging lesion with fair regularity. However, such a focus requires from 6 weeks to 3 months to develop. Once established, it may persist for at least 2 or 3 years. Local cortical freezing produced a loca[illegible] discharging lesion in a matter of hours after application, but the lesion had the disadvantage of disappearing after 7 to 10 days.

The author describes another method of producing chronic epileptogenic alterations. In a series of 66 rabbits and 15 cats, he produced discrete cortical discharging lesions by the application of an ethyl chloride spray to the pial surface. A small bur hole is made over an appropriate area of cortex, and the dura incised and retracted. A fine spray of ethyl chloride is directed onto the pial surface until the underlying cortex whitens and swells up into the cranial opening. The spray is then discontinued, and the dura and overlying scalp tissue closed. Local spike discharges may be observed, beginning from 1 to 3 hours after application. A fairly constant rate of discharge persists for approximately 12 hours, after which the lesions tend to vary in degree of activity from moment to moment. However, even when quiescent in the resting record, the local discharge may be discretely activated by pentylenetetrazol (Metrazol). Evidence of localized paroxysmal activity may persist for up to 3 months in the cat and for at least 6 weeks in the rabbit. The development of a mirror focus, which persists even after ablation of the primary lesion, has been observed in the rabbit. The development of these lesions over time and responses to photic stimulation and to drug administration are described. Histological examination indicates that the lesion may be restricted to 2 mm. of cortical surface and 1 mm. of depth.

Studies in Alcoholism: Effect of Amino Acids on the Rate of Disappearance of Alcohol from the Blood. J. Schiller, R. E. Peck and M. A. Goldberg. A. M. A. Arch. Neurol. 1:127-132 (Aug.) 1959 [Chicago].

The effects of various foodstuffs on the rate of alcohol disappearance from the blood have been investigated in animal and in man. The utilization of glucose to which insulin is added has developed into a therapeutic technique used in the treatment of acute alcoholism. Amino acids administered to experimental animals have seldom been given by infusion, but mainly orally, and rarely as pure amino acids. The oral administration of both alcohol and food has the disadvantage of obscuring the mechanism of action of amino acids on alcohol metabolism. In the investigation reported here, the separation of these 2 factors was obtained by administering alcohol orally and amino acids intravenously.

Ten men with chronic alcoholism hospitalized on closed wards, free of psychosis or physical defects, were selected for this study. Each patient had a battery of liver tests performed, and no subject deviating from the normal standards was considered suitable. No patient was admitted unless he had spent several weeks in the hospital, so as to eliminate any possible alimentary deficiency. Breakfast was not allowed on the morning of the study. Each subject was also kept in bed. Lunch was permitted 3½ to 4 hours after the beginning of the study, since it was considered that all alcohol had been absorbed by that time. A standard dose of 120 ml. of whisky N. F. (100 proof) was ingested within 20 minutes with 1 or 2 oz. (30 or 60 cc.) of water. The amino acids (protein hydrolysates) were used as a 5% solution and were given intravenously by the drip method over a 75-to-90-minute period in quantities of 1,000 ml. Since the amino acid mixtur[illegible] is a solution in 5% dextrose, each patient received in a prior study an infusion of 1,000 ml. of 5% dext[illegible] over a similar period of time, together with 12[illegible] ml. of whisky taken orally. Thus, each patient ser[illegible] as his own control.

It was found that the amino acid mixture decreased the concentration and increased the rate of alcohol disappearance from the blood. The 5% dextrose solution had no such effect. Also, differences in the rates of renal excretion of alcohol were found with the 2 types of infusion. In another group of patients, in whom the amino acid infusion was started one hour after the ingestion of alcohol, it was found that the peaks and rate of utilization of alcohol remained unaffected during the first hour. It was accelerated during the second hour, and the curve took a position intermediate between that produced by dextrose given alone and that by amino acid infusion started after the first hour. Amino acids accelerate the rate of alcohol disappearance from the blood.

PEDIATRICS

The Respiratory Distress Syndrome and Its Significance in Premature Infants. W. A. Bauman. Pediatrics 24:194-204 (Aug.) 1959 [Springfield, Ill.].

The histories of 263 premature infants admitted between December, 1956, and March, 1958, to the premature nursery of Babies Hospital, New York, were reviewed. The study revealed the frequent association of the respiratory distress syndrome in premature infants with pulmonary hyaline membrane formation and death. However, there were also babies who had distress and died but did not have hyaline membrane formation. This indicates that the often fatal respiratory distress syndrome is manifested not only in infants with hyaline membrane formation but also in those with other lethal conditions. Factors such as pulmonary vascular engorgement, metabolic and enzymatic disturbances, neuromuscular underdevelopment, and anatomic interference with respiration should be considered in the study of respiratory distress.

In the series studied, pulmonary hyaline membrane formation occurred more frequently in the smaller and younger infants than in the larger and older ones. The death rate, the frequency of respiratory distress, and the incidence of pulmonary hyaline membrane formation seemed to be in correlation with the premature condition of the infant. Thus, mortality and the incidence of pulmonary hyaline formation were higher in premature infants manifesting intercostal retractions, paradoxical chest and abdominal movements (see-saw respiration), and xiphoid retractions or expiratory grunt than they were in those without these phenomena. The average death rate in the dyspneic infants in the first 7 days of life was 60%; half of those who died had pulmonary hyaline membrane formation. On the other hand, the death rate in premature infants without respiratory distress was 10%, and only a few of these (1 out of 10) had pulmonary hyaline membrane formation. Since a large proportion (40%) of the infants who manifested the clinical syndrome of respiratory distress have survived without treatment, it is advisable that any therapy proposed for this condition should be carefully evaluated before it is used.

Nuclear Sex and Genital Malformation in 48 Cases of Renal Agenesis, with Especial Reference to Nonspecific Female Pseudohermaphroditism. P. J. Carpentier and E. L. Potter. Am. J. Obst. & Gynec. 78:235-258 (Aug.) 1959 [St. Louis].

A chromatin body in the cell nuclei of females is referred to as sex chromatin. The discovery of this chromatin body has been responsible for important advances in the investigation of certain syndromes associated with aberrations in sexual development. Because of the close relationship of the urinary and genital systems in embryologic development and the marked preponderance of males among infants with complete bilateral renal agenesis, genital development and nuclear sex were studied in 48 fetuses and infants presenting this abnormality. They were found in the course of 11,000 autopsies performed at the Chicago Lying-in Hospital. The nuclear sex type was concordant with the external genital sex recorded at birth except in 4 cases which presented a special type of pseudohermaphroditism and were reported in detail. The study indicated that 13 infants were female, and 35 were male. The external genitals were often absent, malformed, or, in some females, markedly masculinized. In the female infants the internal genitals were invariably malformed. Twenty infants in the series presented anorectal malformations, 15 of them having an imperforate anus and an absence of the terminal portion of the intestine. The correlation with external genital malformation was striking. Seven of the 20 infants presented a sirenomelus malformation.

The cases of nonspecific pseudohermaphroditism found in the literature, together with the 4 cases reported here, make a total of 23. The syndrome is probably much more frequent than this would indicate. The authors believe that, in the present state of knowledge, a sharp distinction can be made between "specific" female pseudohermaphroditism due to a fetal or maternal androgenic influence, and not complicated by congenital anomalies, and "nonspecific" female pseudohermaphroditism in which no androgenic influence can be demonstrated but which is accompanied by malformations of other organs. The existence of these 2 distinct types is doubtless related to the chronology and mechanism of the etiological factors involved. If we are to learn more about the etiology of sexual malformation in the human, the gonads, genital organs, and nuclear sex should be systematically studied in every fetus and in every newborn infant, whether

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Specific improvements were observed among these patients in muscular tonus, increase in muscular temperature and thickness, longitudinal growth, recuperation or improvement of reflexes, improvements in muscular movements and physical capacity, and response to faradic or galvanic currents. The time necessary for reaching maximal results varied between 4 to 6 months and several years, according to the number and size of the muscles involved and the degree of disability. Small muscles responded better than large muscles to the treatment. The author is now using a combination of growth hormone, trophic substances, and vitamins, which he believes brings better results in a shorter time.

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The effects of various foodstuffs on the rate of alcohol disappearance from the blood have been investigated in animal and in man. The utilization of glucose to which insulin is added has developed into a therapeutic technique used in the treatment of acute alcoholism. Amino acids administered to experimental animals have seldom been given by infusion, but mainly orally, and rarely as pure amino acids. The oral administration of both alcohol and food has the disadvantage of obscuring the mechanism of action of amino acids on alcohol metabolism. In the investigation reported here, the separation of these 2 factors was obtained by administering alcohol orally and amino acids intravenously.

Ten men with chronic alcoholism hospitalized on closed wards, free of psychosis or physical defects, were selected for this study. Each patient had a battery of liver tests performed, and no subject deviating from the normal standards was considered suitable. No patient was admitted unless he had spent several weeks in the hospital, so as to eliminate any possible alimentary deficiency. Breakfast was not allowed on the morning
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In the series studied, pulmonary hyaline membrane formation occurred more frequently in the smaller and younger infants than in the larger and older ones. The death rate, the frequency of respiratory distress, and the incidence of pulmonary hyaline membrane formation seemed to be in correlation with the premature condition of the infant. Thus, mortality and the incidence of pulmonary hyaline formation were higher in premature infants manifesting intercostal retractions, paradoxical chest and abdominal movements (see-saw respiration), and xiphoid retractions or expiratory grunt than they were in those without these phenomena. The average death rate in the dyspneic infants in the first 7 days of life was 60%; half of those who died had pulmonary hyaline membrane formation. On the other hand, the death rate in premature infants without respiratory distress was 10%, and only a few of these (1 out of 10) had pulmonary hyaline membrane formation. Since a large proportion (40%) of the infants who manifested the clinical syndrome of respiratory distress have survived without treatment, it is advisable that any therapy proposed for this condition should be carefully evaluated before it is used.

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Ten men with chronic alcoholism hospitalized on closed wards, free of psychosis or physical defects, were selected for this study. Each patient had a battery of liver tests performed, and no subject deviating from the normal standards was considered suitable. No patient was admitted unless he had spent several weeks in the hospital, so as to eliminate any possible alimentary deficiency. Breakfast was not allowed on the morning of the study. Each subject was also kept in bed. Lunch was permitted 3½ to 4 hours after the beginning of the study, since it was considered that all alcohol had been absorbed by that time. A standard dose of 120 ml. of whisky N. F. (100 proof) was ingested within 20 minutes with 1 or 2 oz. (30 or 60 cc.) of water. The amino acids (protein hydrolysates) were used as a 5% solution and were given intravenously by the drip method over a 75-to-90-minute period in quantities of 1,000 ml. Since the amino acid mixture is a solution in 5% dextrose, each patient received in a prior study an infusion of 1,000 ml. of 5% dextrose over a similar period of time, together with 120 ml. of whisky taken orally. Thus, each patient served as his own control.

It was found that the amino acid mixture decreased the concentration and increased the rate of alcohol disappearance from the blood. The 5% dextrose solution had no such effect. Also, differences in the rates of renal excretion of alcohol were found with the 2 types of infusion. In another group of patients, in whom the amino acid infusion was started one hour after the ingestion of alcohol, it was found that the peaks and rate of utilization of alcohol remained unaffected during the first hour. It was accelerated during the second hour, and the curve took a position intermediate between that produced by dextrose given alone and that by amino acid infusion started after the first hour. Amino acids accelerate the rate of alcohol disappearance from the blood.

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alive or dead, whenever congenital malformations are discovered. Even the most macerated fetus is worthy of careful investigation. The desirability of thorough inspection of the perineum in every newborn infant cannot be overemphasized. The passage of meconium through the urethra in the absence of an anal opening is an indication that a rectovesical fistula is present. It should be kept in mind that in such infants, as well as in those with urethrovaginal fistulas, urinary infection is a frequent and dangerous complication. The differential diagnosis between "nonspecific" pseudohermaphroditism and the adrenogenital syndrome may be difficult. Genital malformation, vomiting, and dehydration occur in both, but in the adrenogenital syndrome associated malformations are lacking. Consequently, when such symptoms are present, a careful search must always be made for the possible presence of other malformations.

Chronic Type of Severe Idiopathic Hypercalcemia: Treatment with Thyroxin. C. Hooft and A. Vermassen. Acta paediat. belg. 13:57-74 (no. 2) 1959 (In French) [Brussels].

The authors report on a one-year-old female infant with chronic and severe idiopathic hypercalcemia of the Fanconi-Schlesinger type. The child exhibited the classic symptoms of anorexia, vomiting, failure to thrive from birth, constipation interrupted by attacks of diarrhea and dehydration, retardation of both physical and mental development, marked muscular hypotonia, characteristic face with large ears, flat bridge of the nose, convergent strabismus, receding mandible, small head circumference, hypertension, and a low systolic murmur. The most important biochemical findings were persistent hypercalcemia, hypercholesteremia, and impaired renal function. Roentgenograms revealed hypercalcification of the bones, as manifested by dense transverse bands in the metaphyses of the long bones and increased density at the base of the skull.

The first clinical manifestations of the hypercalcemia, i. e., anorexia, vomiting, and failure of normal growth, were observed soon after birth and with certainty before the administration of vitaminized milk and supplementary doses of vitamin D. The patient received 600,000 units of vitamin D for the first time at the age of 6 months; this caused increased symptoms and loss of weight and established the presence of an increased sensitivity to vitamin D. It has, therefore, been suggested that the Fanconi-Schlesinger type of idiopathic hypercalcemia results from a metabolic abnormality of endogenous vitamin D-active substances (probably sterols).

Treatment with thyroxin was instituted in this infant with doses of 1 mg. every second day; after one month the dose was increased to 1 mg. every day, and it resulted in a clear-cut improvement of all the clinical, biochemical, and roentgenologic features. The favorable effect of this treatment was not due to hypofunction of the thyroid (which had not been observed clinically in the patient), but resulted probably from increased excretion of calcium, both in the urine and in the feces. Thyroxin may have a direct effect on the vitamin D activity of the serum.

Congenital Nephrotic Syndrome. N. Hallman and L. Hjelt. J. Pediat. 55:152-162 (Aug.) 1959 [St. Louis].

The authors report the clinical course and the postmortem findings in 18 infants with the congenital nephrotic syndrome. The infants came from 12 families with a total of 49 children. Thus, one-third of the children from these families were affected with this syndrome. Eleven infants of these sibships, who were born prematurely, died in the newborn period. The authors feel tempted to correlate the unusual high incidence of prematurely born children and death with the nephrotic syndrome of other children in the families. Familial occurrence suggests an hereditary origin of the disease, although no evidence to support this possibility could be found. With 3 exceptions, the infants with congenital nephrosis were born 3 to 5 weeks prematurely, and the size of the infants was relatively small. The placenta was larger and heavier than usual in the majority of cases. Edema frequently occurred immediately after birth and was present in all the infants by 2 months of age by which time proteinuria was pronounced. Changes in the urine and plasma proteins were typical of the nephrotic syndrome. In the initial phase of the disease no erythrocytes were found in the urine, although some appeared later. The blood urea nitrogen level was low, as was the blood pressure. The plasma cholesterol level was often under 200 mg. per 100 cc., but it rose consistently as the disease progressed. The serum fat curve after intravenous injection of a fat emulsion was also typical of the nephrotic syndrome.

With the exception of one child, who is now 8 months of age and is still suffering from the disease, all the infants have died, the oldest at the age of 19 months. Postmortem examinations showed the kidneys to have changes typical of the nephrotic syndrome. In the patients who died at earlier ages, the changes in the basement membranes of the glomerular capillaries were mild; more numerous proliferative changes were found in the patients dying later. Fatty degeneration was always present in the cells of the tubules. The absence of typical foot processes and of splitting of the basement membranes was established by electron microscopy in 3 cases. The tubules had a thickened basement membrane which was lamellar in structure.

Prolonged Neonatal Anoxia Without Apparent Adverse Sequelae. C. C. Mabry. J. Pediat. 55:211-215 (Aug.) 1959 [St. Louis]

The author reports on a prematurely born infant who survived a prolonged period of asphyxia with no demonstrable heart beat. The infant was born to a 19-year-old woman after a gestation period of about 35 weeks. Fetal heart sounds were heard until near the time of delivery and a viable infant was expected. However, a child weighing 3 lb. and 4 oz. (1,473 Gm.) was delivered, in whom there were no manifestations of life. Resuscitation was started immediately, but after 15 minutes there was no sign of success. The infant was declared "stillborn" and taken to a nearby room for demonstration of resuscitation techniques; these were started 25 minutes after the infant was born. An endotracheal tube was inserted, and the lungs were inflated by the expired air of 3 separate operators. Thirty minutes after delivery a pulse was first detected in the umbilical cord, and a slow, irregular, weak heart beat was heard with the stethoscope. Resuscitation was continued, and 30 mg. of caffeine and sodium benzoate was administered intramuscularly. The infant first gasped at the age of 40 minutes and began to breathe regularly and spontaneously at 60 to 65 minutes. He was then transferred to an Isolette with oxygen (38 vol. %) and received additional supportive care, consisting of gavage feeding and antimicrobial therapy (chloramphenicol). After the first week special premature infant care became unnecessary, and the child's course during the remaining 5 weeks in the nursery was characterized by steady growth and development. He has now reached the age of 20 months and has demonstrated average development.

The survival of an anoxic newborn infant is probably dependent on the enhanced ability of the brain at birth to utilize an anaerobic type of glycolysis. This phenomenon was first suspected when it was shown that the metabolic rate, as measured by oxygen uptake, within the immediate neonatal period is lower than it is in the adult. The persistence of circulatory function and reduction in body temperature are other critical factors protecting the newborn infant from changes induced by anoxia. Alterations in body temperature occur at birth, and there is considerable evidence that reduced body temperature ameliorates the effect of anoxia neonatally. Other authors have demonstrated in asphyxiated guinea pigs a linear increase in the time of survival of approximately 50% per 10 C decrease in body temperature when compared with that of noncooled controls. The explanation offered for this observation is that the cellular metabolic rate decreases with decreasing temperature, thus reducing the oxygen requirement. In the case reported here, the first body temperature recorded was obtained at the age of 12 hours and was 35 C (95 F). Although the infant's temperature was probably reduced prior to being revived and during the first hours of life, his actual body temperature probably did not approach the extreme levels of cold.

The Phases of "Transitional Distress" Occurring in Neonates in Association With Prolonged Postnatal Umbilical Cord Pulsations. M. M. Desmond, J. L. Kay and A. L. Megarity. J. Pediat. 55:131-151 (Aug.) 1959 [St. Louis].

The authors describe the clinical courses of 41 infants with prolonged pulsations of the umbilical arteries after delivery, who were seen over the period of a year at the Jefferson Davis, Hermann, and St. Luke's hospitals in Houston, Texas. The mean duration of cord pulsation was 5 hours, with a range of from 40 minutes to 13 hours after birth. Thirty-eight of the 41 infants showed evidence of disturbance in transition to extrauterine life. The disturbed period of transition appeared to be initiated by (1) a disease within the infants (intrinsic or intrafetal disease) or (2) an adverse influence in the extrauterine environment (extrinsic or extrafetal disease) or by a combination of the two. Five infants died within 11 hours of birth because of this disturbance.

Regardless of the major or presenting symptoms of the infants with extrinsic disease, the total symptomatology (transitional distress) followed a general sequence, which could be divided into 3 phases according to cardiopulmonary and neurological manifestations. In phase 3, respiration progresses from slow, gasping respiration to labored grunting and finally to a more rapid rate. The heart rate progresses from a bradycardia to a normal rate, and parasympathetic effects predominate at the level of greatest depression. In phase 2, the respiration is rapid, shallow, and regular, and the heart rat transiently increases. As the rapid respiratory rat begins to decline, the patient may either progre directly to phase 1 or exhibit evidences of neur excitation. In phase 1, respiration and cardiac a tivity gradually return to the lability characteristi of the neonate, and the neurological behavio approaches the normal. Infants with extrinsic disease who appeared to be improving clinically followed a sequence from phase 3 to phase 2 to phase 1; infants who appeared to be deteriorating clinically followed the same sequence of symptomatology in reverse order.

Infants with intrinsic disease and superimposed hypoxia followed a similar sequence as they were improving or deteriorating clinically. The sequence of phases seen in infants deteriorating clinically is similar to that seen in progressive cerebral depression and the sequence in infants whose condition is improving resembles that of recovery from depression. It may, therefore, be postulated that infants undergoing these sequences are undergoing, respectively, depression or recovery of the neuraxis. The maternal histories and the histories of labor and delivery support this assumption, since 86% of these pregnancies and deliveries had complicating factors, and 73% of the infants either had fetal distress before delivery or were in poor condition at the time of birth. The complications encountered during phase 3 were atelectasis, hyaline membrane disease, and congestive failure; apnea, seizures, and vomiting occurred during phase 2; and jaundice occurred during both phase 2 and phase 1.

Prolonged pulsation of the umbilical vessels is one of the physical signs occurring during the phases of transitional distress. It is postulated that umbilical arteries may pulsate after delivery because of a decreased contractility of the musculature brought about by anoxia or asphyxia. Hemorrhage from the umbilical arteries may occur in association with umbilical cord pulsations. The onset of hemorrhage may be abrupt, occurring at the beginning of the phase of neural excitation.

The Neonatal Icterus Form of Minkowski-Chauffard Disease. M. LeLong, D. Alagille and J. Dormont. Arch. franç. pédiat. 16:577-598 (no. 5) 1959 (In French) [Paris].

It has generally been considered that hemolytic jaundice (Minkowski-Chauffard syndrome) is only revealed several years or more after birth. The authors wonder if this symptomatic silence in infancy is not more apparent than real, and if a neonatal icterus could reveal the disease in a certain number of cases. They report 5 observations on the congenital, familial, hemolytic form of the Minkowski-Chauffard syndrome with neonatal icterus. They also cite 9 comparable observations drawn from the literature. In the majority of the observations, icterus has appeared early—within the first 24 hours and frequently even from the 12th hour. The intensity of this type of icterus easily differentiates it from simple icterus. Sometimes it appears early and regresses within a short time. The liver and the spleen are generally normal during the neonatal period. Splenomegaly inconsistently appears in the following weeks or months. Bilirubinemia has an indirect predominance. When the bilirubin value surpasses 180 to 200 mg. per 100 cc., nervous complications are very possible, and exchange transfusion should be practiced without delay.

The 2 main positive indicative criteria of the Minkowski-Chauffard syndrome are familial antecedents and blood signs indicating a cellular defect. The existence of this syndrome in other members of the family is an important consideration which calls for study. This factor was found in the 9 observations drawn from the literature and in 3 of the authors' observations. However, in one of the authors' cases, the mother and grandmother were proved to be carriers, although they had no clinical signs and the defect was demonstrated only in 2 distant cousins. In another case, the defect was not known in the family, and blood examinations of the close relatives did not disclose even minor anomalies. There are other blood diseases related to hereditary cellular defects which have a clinical picture very similar to that of the Minkowski-Chauffard syndrome. Spherocytosis, diminution in the average diameter of the red blood cells, anomalies of the Price-Jones curve, presence of rouleaux, and irregular and small red blood cells are among the defects which can sometimes be seen during the first hours of life. Increase of osmotic fragility is even more indicative, provided that it is unmistakable, but it is often not present during the neonatal period, and diagnosis at birth is difficult. Fetal-maternal blood incompatibilities (particularly of the ABO type) must be eliminated as a cause. Often a diagnosis, suspected only during the neonatal period, is confirmed later.

Exchange transfusion, simple transfusion, and splenectomy are therapeutic initiatives. A high rate of bilirubinemia entails a risk of serious and irreversible lesions of the nervous system and is one of the most important indications for exchange transfusion. Weight at birth and age of the child intervene in the decisions. A newborn infant of normal weight can have transfusion after the 4th day, and a premature baby after the 6th day. Transfusion can help in the transitory phase when anemia is partially due to a medullary hypoactivity. It is indispensable in persistent anemia and when splenectomy must be deferred. The major arguments in favor of early splenectomy are the possibility of serious anemia resulting from severe hemolysis with or without medullary hypoplasia and the risk of disturbance of weight-height and motor development. The arguments against early splenectomy are risk of postoperative infectious accidents of meningitis or septicemia type. This risk should be carefully studied in each case. It may be preferable to delay such an intervention until the end of the first year.

Patent Ductus Arteriosus of the Newborn: Diagnosis, Operative Indications and Results: Based on 55 Observations. M. Thibert, J. Binet, P. Lucet and J. Nouaille. Arch. franç. pédiat. 16:619-632 (no. 5) 1959 (In French) [Paris].

Fifty-five observations on infants with patent ductus arteriosus are reported; in 37 of the cases the condition was accompanied by pulmonary hypertension. Since simple patent ductus arteriosus is perfectly tolerated and does not present any diagnostic problem, only 4 infants with this form were operated on before the age of 2 years. However, when the disease is accompanied by hypertension, it is serious. Children with this combination of disorders are hypotrophic and dyspneic, and frequently have pulmonary accidents which are often accompanied by signs of cardiac failure. Clinical diagnosis depends on the existence of a systolic (or continued) murmur located high, vigorously beating peripheral arteries, enlarged heart, lungs which are overloaded with blood, and an electrocardiogram showing a biventricular overloading. Catheterization alone assures an accurate diagnosis. It should be done systematically in every newborn child who has a cardiopathy with a badly tolerated left-right shunt. Patent ductus arteriosus is the only one of these malformations which is easily accessible to surgery at a very young age.

Twenty-seven infants with patent ductus arteriosus and hypertension were operated on before the age of 2 years. Pulmonary and aortic pressures were registered as much as possible before and after clamping of the duct, which gives a basis for prognosis. There were 5 operative deaths, all in infants who had very high pulmonary pressures and another cardiac anomaly as well as the patent ductus arteriosus. Twenty-one children were seen again after a sufficient lapse of time. In every case except one, functional signs and pulmonary episodes had disappeared. The hypotrophic condition of the children regressed during the months which followed the intervention, the heart diminished in volume, and pulmonary overloading disappeared. Among these 21 results, one was ineffectual, another was incompletely satisfactory, but 19 were very good.

UROLOGY

Hormone Excretion in Prostatic Cancer: The Early and Late Effects of Endocrine Treatment on Urinary Oestrogens, 17-Ketosteroids and 17-Ketogenic Steroids. R. D. Bulbrook, L. M. Franks and F. C. Greenwood. Acta endocrinol. 31:481-499 (Aug.) 1959 [Copenhagen].

The studies described aimed to answer the following questions: 1. Does the urinary excretion of estrogens and 17-ketosteroids in men with untreated prostatic cancer differ from that of men of the same age without clinical cancer? 2. What changes occur in hormone excretion within the first 2 years of treatment by castration or synthetic estrogens, and is there any correlation between these changes and the clinical state of the patient? 3. What changes have occurred in patients who have survived for more than 5 years after treatment, and are these changes associated with the clinical state? Four groups of patients were studied. The diagnosis of prostatic cancer was confirmed microscopically, and the patients were admitted to hospital for the collection of 24-hour urine specimens. Twenty-two men (group 1), admitted to hospital for cardiac, cerebral, or pulmonary conditions but without gross endocrine or genitourinary disease, served as controls. Group 2 included 18 patients with untreated prostatic cancer; group 3 included 8 men with prostatic cancer treated by castration or synthetic estrogens for less than 2 years; and group 4 included 7 men with prostatic cancer treated with synthetic estrogens for more than 5 years.

It was found that the excretion of estrogens, 17-ketosteroids, and 17-ketogenic steroids in patients with untreated prostatic cancer does not differ from that of men of similar age without clinical cancer. The excretion of these hormones is depressed by castration or treatment with synthetic estrogens, but in most cases there is a rise, beginning within 6 months, to pretreatment levels. This biphasic response is shown most clearly by the estrogens. Objective regression of tumor growth is associated with depression of hormone excretion in these cases. The later rise in excretion is generally followed by renewed tumor growth. The excretion of estrogens and 17-ketosteroids is lower than normal in patients surviving for 5 years or more after treatment with synthetic estrogens. In these cases excretion may remain low even in relapse. There is, therefore, an apparent correlation between the level of excretion of the hormones measured and tumor activity, within the first 2 years of treatment. In patients surviving 5 years or more, there is no such correlation. Other factors must also be involved in tumor growth in these cases. All the hormones measured in this study are produced in response to stimuli from trophic anterior pituitary hormones, and changes in excretion probably reflect changes in pituitary function. The basic endocrine factor associated with prostatic cancer may, therefore, be of pituitary origin.

Diagnosis of Malignancy of the Prostate with Needle Biopsy. W. K. Hicks and D. E. Howard. J. Iowa M. Soc. 49:522-525 (Aug.) 1959 [Des Moines].

Cancer propaganda and the conscientiousness of the general practitioner are the 2 big factors in the early diagnosis of prostatic malignancy. The cancer propaganda must induce men over 45 years of age to get a yearly checkup. The general practitioner must include a rectal examination in that checkup, and he must recognize and have a study made of any areas of hardness or irregularity in the prostate. The authors first used the Silverman needle and later the Franklin modification of that needle in making biopsy studies of suspicious prostatic lesions. The technique used consists of puncturing perineally, then guiding the needle along the anterior wall of the rectum with the finger in the rectum. With the nodule in the prostate resting on the finger tip, the needle is guided up to it, and then the split core is pushed into the nodule. Two to 4 specimens are removed. Recently, the transrectal approach has been used. Some areas will be reached more readily by the transperineal route, and others are more accessible by the transrectal approach. The patient comes to the hospital without breakfast. The biopsy is done, preferably, under a low-spinal-block anesthesia. After the biopsy, a small catheter is left indwelling until evening or the following morning. The patient is home after 12 or 24 hours.

The authors determined the accuracy of this method in 105 needle biopsies on 96 patients with suspicious prostatic lesions. Fifty-seven of the 96 patients had intracapsular lesions, in which cure is possible, whereas in those with extracapsular lesions, local spread, and metastases, only palliative treatment is called for. The authors are concerned chiefly with the 57 intracapsular lesions. Biopsy revealed malignancy in 22 of these patients. As proved by later studies, the 22 positive biopsies were 100% correct. Of the 35 patients who had negative biopsies on the first needle punch, one has since died of a cause unrelated to the urinary tract, and another has been lost sight of. In 2 of the remaining 33 patients, carcinoma was detected on a second needle biopsy, and in a third patient, for whom a second biopsy was again negative, the diagnosis of prostatic cancer was made from tissue removed at the time of a transurethral prostatic resection. In all 3 patients the diagnosis was made early enough to permit radical retropubic prostatectomy, and they are free of signs of cancer at the present time. None of the remaining 30 patients with negative biopsies have shown signs of prostatic cancer. Thus, 30 of 33 negative needle biopsies were correct (90%).

OPHTHALMOLOGY

Mycotic Ulcerative Keratitis. B. Anderson, S. S. Roberts Jr., C. Gonzalez and E. W. Chick. A. M. A. Arch. Ophth. 62:169-179 (Aug.) 1959 [Chicago].

The authors report on 5 men, between the ages of 33 and 47 years, with ulcerative mycotic keratitis. There was a history of an abrasion, a laceration, or a foreign body. A fluffy white, slightly elevated protuberance appeared at the site of the initial injury. The superficial layers of the immediately surrounding cornea seemed to liquefy, forming a shallow crater. Surrounding this crater, a wide, grayish, rather sharply demarcated halo formed. The mounded central white core assumed a somewhat laminated appearance, which persisted for weeks after eradication of the fungi, becoming compressed into a tenacious white plaque. This corneal ulcer proved refractory to treatment with antibiotics that would have been expected to sterilize a bacterially infected lesion. During this refractory period, pathogenic bacteria had not been cultured from these eyes. The fungi, which were observed in smears and cultures from the lesions, included Penicillium sp., Aspergillus versicolor, Fusidium terricola, Gibberella fujikuroi, Curvularia lunata, and a corn smut. These fungi disappeared when the eyes were treated with amphotericin B. Regression and healing of the ulcers occurred coincidentally with the eradication of the fungi, and lamellar grafts were successfully employed in preserving the integrity of the globe.

These observations indicate that mycotic infections of the eye are becoming more frequent. This increasing incidence coincides with the increased use of combined antibiotics and corticosteroids. The history and appearance of these lesions have, in common, characteristics which greatly aid in a clinical etiological diagnosis. Amphotericin B and keratoplasty have been effective in the treatment of this condition.

Some Neuro-Ophthalmological Considerations in Cerebral Vascular Insufficiency: Carotid and Vertebral Artery Insufficiency. W. F. Hoyt. A. M. A. Arch. Ophth. 62:260-272 (Aug.) 1959 [Chicago].

Progressive occlusion of the extracranial portion of the major cerebral vessels is now recognized as an important cause of strokes. Advances in vascular surgery have made possible the improvement of cerebral blood flow in patients with intermittent cerebral vascular insufficiency. Recognition of the prodromal symptoms of obstruction of the extracranial portion of the carotid and vertebral arteries is important if patients are to be treated before a frank stroke occurs. Transient visual symptoms occur frequently in patients with intermittent insufficiency of the extracerebral portions of the carotid and vertebral arteries. Transient monocular visual loss is the hallmark of carotid insufficiency. Attacks of monocular blindness in patients with carotid disease may last as long as 10 minutes; yet permanent visual loss is seldom observed.

The retina seems to be a sensitive indicator of insufficiency of carotid blood flow in some patients. In the group of patients who have carotid insufficiency but do not have attacks of monocular blindness, collateral circulation to the ophthalmic artery must be sufficient to preclude attacks of retinal ischemia. Transient hemianopsia is rarely a part of the carotid insufficiency syndrome. In the usual patient with intermittent carotid insufficiency, examination of the eye, with the exception of ophthalmodynamometry, gives entirely normal results. The pupillary light reflex is absent during an attack of monocular blindness. A bruit audible over the eye, and sometimes audible to the patient, may be one of the earliest signs of carotid insufficiency. Between attacks of blindness, ophthalmoscopic examination of the ocular fundus is routinely unimpressive. Ophthalmodynamometric measurement provides one of the few objective ophthalmological findings in the carotid insufficiency syndrome, showing a reduction of 15 to 25 mm. in the diastolic pressure in the ophthalmic artery on the side of the involved carotid artery.

Transient bilateral blurring of vision, or loss of vision, and diplopia are the 2 types of visual disturbance which occurs in the syndrome of intermittent insufficiency of the vertebral system. Objective ocular findings are usually absent. During an attack, horizontal-rotatory nystagmus, ptosis, or pupillary changes may be noted. The brief duration of these attacks, however, almost precludes the opportunity for the physician to witness them. Ophthalmodynamometry is of little value in intermittent insufficiency of the vertebral system except to exclude the possibility of coexisting carotid insufficiency.

In patients in whom intermittent insufficiency of either the carotid or the vertebral system occurs singly, the clinical diagnosis is usually not difficult. However, atheromatous disease of arteries is most often a scattered disseminated process. Obstructive arterial changes occurring in both systems simultaneously create a difficult diagnostic problem, since a symptom belonging to the carotid insufficiency syndrome, such as transient mononuclear blindness, can appear with symptoms of vertebral insufficiency. To conclude that both systems are involved, on clinical grounds alone, is not possible. Arteriography of both carotid and vertebral systems, including the aortic arch, may be the only way to define the problem. Because of the many visual symptoms which occur, the specialized knowledge of the ophthalmologist can contribute significantly to the over-all evaluation of this interesting group of patients with cerebral vascular insufficiency. History, physical examination, cerebral blood flow studies, ophthalmodynamometry, and arteriography are all necessary for a detailed understanding of each patient's problem.

Ocular Manifestations of Pituitary Tumor in Cushing's Syndrome. T. P. Kearns, R. M. Salassa, J. W. Kernohan and C. S. MacCarty. A. M. A. Arch. Ophth. 62:242-247 (Aug.) 1959 [Chicago].

Of 122 patients with adrenal hyperplasia and adrenal cortical hyperfunction (Cushing's syndrome) studied at the Mayo Clinic between 1945 and 1958, 4 women and 2 men, between the ages of 28 and 60 years, had clinical or histological evidence of pituitary tumor. Ocular symptoms were present in these 6 patients, 5 of whom had visual field defects of a chiasmal nature and 4 had palsy of the third cranial nerve. The incongruous homonymous nature of the changes in the visual fields, rather than the more usual bitemporal hemianopsia, and the involvement of the third cranial nerve indicated parasellar extension of the tumor. This feature and, in addition, the rapid onset of symptoms have suggested that the pituitary tumors associated with Cushing's syndrome are more active cellularly than is usually the case in patients without Cushing's syndrome. Histological study of the pituitary tumors was possible in all 6 patients, the tissue being obtained at craniotomy in 5 and at autopsy in 1; all the tumors were chromophobe adenomas.

From these observations, it appears that roentgenographic study of the sella should be routine in the initial examination and subsequent evaluation of patients who have Cushing's syndrome. Ophthalmoscopic examinations should be done in all such patients. Visual fields should be plotted when any question exists regarding pituitary tumor. Extracranial metastasis of a pituitary tumor is extremely unusual, but this possibility should be considered when one is dealing with a pituitary tumor in a patient who has Cushing's syndrome.

Ocular Lesions in Collagen Diseases and Their Treatment with Prednisolone. J. F. Castiglione. Prensa méd. argent. 45:348-350 (Feb. 5) 1959 (In Spanish) [Buenos Aires].

Ocular lesions occur in a high percentage of patients suffering from collagen diseases. In such cases the therapeutic use of prednisolone shortens the course of the total condition and helps the restoration of vision, especially if administered as soon as these ocular complications are detected. As this steroid has a greater anti-inflammatory activity than either cortisone or hydrocortisone, it can be administered in smaller doses and does not cause alterations in the water-salt and protein metabolism. The author reports on 20 cases of collagen disease associated with different types of ocular complications. This series, composed of 11 men and 9 women, included 5 patients with keratitis, 4 with conjunctivitis, 4 with corneal ulcer, 2 with episcleritis, 3 with keratitis and corneal ulcer, and 2 with scleritis and keratitis. Prednisolone was administered to each patient in daily amounts of 20 to 30 Gm., divided into smaller doses taken every 4 to 6 hours, preferably after meals. The total dose given varied from 100 to 500 mg., and the duration of treatment ranged from 4 to 20 days. The therapy was well tolerated, and the results were very good in 11 patients, good in 8, and poor in only one.

THERAPEUTICS

Development of Sensitivity to Penicillinase Following Its Use in Penicillin Reaction. R. C. Weiss and S. B. Crepea. J. Allergy 30:337-341 (July-Aug.) 1959 [St. Louis].

Penicillinase, an enzyme derived from various bacterial sources, is a protein with a molecular weight of about 50,000. It acts by catalyzing the hydrolysis of the lactam ring of penicillin to penicilloic acid, a substance devoid of antibacterial activity. Initial studies suggested its value in treating penicillin sensitivity reactions. The authors describe studies on 8 patients with penicillin reactions of the serum sickness type. They were given 800,000 units of penicillinase intramuscularly. In addition, each was tested intradermally with the following mixtures: penicillin in isotonic sodium chloride solution, 500 units per cubic centimeter; penicillinase in concentrations of 5,000 and 10,000 units per cubic centimeter; penicillin, 500 units, plus penicillinase, 5,000 units per cubic centimeter; and penicillin, 1,000 units, plus penicillinase, 10,000 units per cubic centimeter. Where possible, these tests were performed before penicillinase administration and again 2 or 3 weeks later. Ten nonsensitive persons were similarly tested as controls. It was found that in 4 of 8 patients positive skin sensitivity developed from a single injection of 800,000 units of penicillinase. The tests in the 10 nonsensitive persons were all negative.

By destroying the penicillin molecule, penicillinase theoretically inhibits further reaction. However, the demonstrated antigenicity of penicillinase in both human and animal experiments suggests caution in its use. The repeated injection of the drug under certain clinical conditions could result in serious anaphylactic reactions. Similarly, in addition to this potential hazard, the experimental demonstration of the development of antipenicillinase antibodies could well result in decreased effectiveness of penicillinase activity. In some instances penicillinase fails to destroy entirely the antigenicity of penicillin in vitro (2 patients in the group of 8), and this may occasionally explain therapeutic failures.

Results of Calcic Phenylbutazone Associated with Prednisone in Rheumatology. F. Nebó and G. Spilborghs. Rev. Assoc. med. brasil. 5:164-169 (April-June) 1959 (In Portuguese) [São Paulo, Brazil].

The practical interest of the combined phenylbutazone-prednisone therapy is the possibility of reducing the usual doses of both drugs, thus reducing their toxic effects. The authors report 15 cases of rheumatism in which this combined therapy was administered. There were 14 females and 1 male in the series. With the exception of a 9-year-old, all the patients were adults between the ages of 18 and 62 years. There were 9 cases of rheumatoid arthritis, 3 of infectious arthritis, 2 of arthritis associated with osteoarthrosis, and 1 of simple osteoarthrosis. Once the clinical diagnosis had been confirmed by laboratory tests, and after an interval of 7 to 10 days following the last administration of any other drug, the combined phenylbutazone-prednisone therapy was instituted. The daily doses were 3 tablets (6 mg.) of prednisone and 300 mg. of phenylbutazone, except for one patient who received 2 tablets of prednisone (4 mg.) and 200 mg. of phenylbutazone daily. The total doses reached a minimum of 45 tablets (90 mg.) of prednisone and 4,500 mg. of phenylbutazone, and a maximum of 375 tablets (750 mg.) of prednisone and 37,500 mg. of phenylbutazone.

In 3 patients the rheumatic condition remained unchanged. In 2 there was a slight improvement, i. e., the laboratory tests were better, although there was no definite improvement of the articular pain. Seven patients experienced definite improvement, i. e., there was functional recuperation of the joints involved, disappearance of the articular pain, and improvement in the general condition. In 3 patients the improvement was very marked, with complete return of functional ability, disappearance of pain, redness, heat, and edema, together with important changes in the laboratory tests. The side-reactions were mild and easily controlled. The results were encouraging with the combined therapy. Although the rheumatic lesions suffered by the 15 patients were irreversible, most of them experienced a noticeable improvement in their symptoms and functional recuperation of their joints.

Treatment of Plasmocytoma with Prednisolone. F. Thedering and R. Vüllers. Blut 5:161-165 (July) 1959 (In German) [Munich, Germany].

The authors report on 4 patients with beta-plasma cell myeloma and on 3 patients with gamma-plasma cell myeloma, who were treated with prednisolone in the department for internal diseases of the Pius Hospital in Oldenburg, Germany. The patients were first given an initial dose of 30 to 40 mg. of the steroid for 8 to 14 days, and maintenance treatment was practiced with doses of 15 to 25 mg. for the following weeks up to 4 months. Skeletal pain was the predominant symptom in 6 of the 7 patients, and relief of such pain was obtained in 5 of these. There was improvement of the general condition and gain in weight. Bence-Jones proteinuria was reduced in 5 patients. Reduced retention of urea and creatinine served as proof of improved retinal function. All 7 patients had normochromic anemia, with hemoglobin values between 31 and 60%, when administration of prednisolone in small doses was started, and blood transfusions were required despite repeated small increases in the number of reticulocytes. Blood transfusions were no longer required in 3 patients who received doses of 60 mg. of prednisolone for 3 or 4 weeks or who were given initial massive doses of 200 to 250 mg. daily. An increase of the hemoglobin level to values varying between 60 and 80% was noted after an increase in the number of reticulocytes. In only 1 of the 7 patients, however, was the severely disturbed protein metabolism restored to normal, and this patient also regained his full work capacity.

Four patients died, and the duration of their disease varied from 7 to 17 months. The 3 surviving patients have been followed for 3 to 20 months. These findings do not suggest that prednisolone therapy prolonged the life of the patients, but despite that this therapy is to be considered valuable. Undesirable side-effects, such as osteoporosis, pathological fractures, and an increased susceptibility to infections, were more frequent with administration of initial doses of 250 mg. and maintenance doses of 50 to 60 mg. than with the initial doses of 50 to 60 mg. and maintenance doses of 25 mg.

Some Cardiovascular Effects of Phenyl-2-Butyl-Norsuprifen Hydrochloride (Arlidin). F. S. Caliva, R. Eich, H. L. Taylor and R. H. Lyons. Am. J. M. Sc. 238:174-179 (Aug.) 1959 [Philadelphia].

The cardiovascular effects of Arlidin were studied by various techniques. Parenteral administration of the drug was found to increase cardiac output an average of 34% and to decrease peripheral resistance by 23%. Blood flow to the skin was not affected, although calf flow increased about 30%. This rise in calf flow most probably represents an increase in blood flow to the muscle. Arlidin is apparently safe in the absence of organic heart disease. No untoward side-effects were observed, and the effects on the heart rate and blood pressure were minimal. Treadmill studies, however, failed to show that the drug had any significant effect on intermittent claudication, and this leaves its practical value in this condition open to question.

Liothyronine (L-Triiodothyronine) as Replacement for Thyroid Hormone. R. Finkler. J. Am. M. Women's A. 14:593-594 (July) 1959 [New York].

Liothyronine was administered to 166 hypothyroid patients during the past 3 years. These patients were treated in private practice. All had a low basal metabolic rate and one or more of the following symptoms of hypothyroidism at the time liothyronine therapy was started: obesity, menstrual irregularities, chronic fatigue, vague aches and pains, dry skin and hair. Ninety-five patients had not received previous thyroid therapy, and 71 had received either desiccated thyroid or thyroglobulin. The 71 patients discontinued use of these preparations for one week or longer before they were started on liothyronine therapy. Pretreatment laboratory measurements of protein-bound iodine and serum cholesterol levels were made in about 30% of the patients and were comparable to those usually obtained from a group of hypometabolic patients. In 11 representative patients, protein-bound iodine and serum cholesterol measurements were made both before therapy with liothyronine and at the optimum dosage. Four of these patients had previously received desiccated thyroid. Data on these 11 patients are tabulated.

Symptoms of hypothyroidism were ameliorated or eliminated in the 95 patients who had not received previous treatment with thyroid hormone. Obese patients who had reached a "plateau" in their loss of weight began to lose weight again; menstrual regularity was achieved in patients who had complained of irregularities; and patients who had complained of fatigue felt less fatigued and were more active. In addition, dry skin and hair conditions improved, and patients no longer complained of vague aches and pains. Fifteen of the 71 patients who had received thyroid therapy previously experienced additional improvement on liothyronine therapy; the conditions of the others were maintained as well on liothyronine. The author concludes that liothyronine may be used whenever thyroid hormone is indicated. It often benefits patients who do not respond well to ordinary thyroid preparations. Optimum dosage may be established more rapidly with liothyronine than with thyroid, and the incidence of side-effects may be lower than with desiccated thyroid of L-thyroxin.

The Intra-arterial Route for the Introduction of Radioactive Isotopes into the Kidney: Experimental Research. F. Morino. Minerva med. 50:2137-2144 (June 27) 1959 (In Italian) [Turin, Italy].

An experimental study made on 23 large dogs, weighing 20 to 25 kg. (44 to 55½ lb.) each, in connection with the intra-arterial administration of radioactive isotopes into the kidney, is reported. The animals were divided into 3 groups, composed of 10, 7, and 6 dogs respectively. Radiogold (Au^{198}) adsorbed in carbon powder was used in the 10 animals of the first group, radioyttrium (Y^{90}) in a granule suspension was used in the 7 animals of the second group, and colloidal Au^{198} was used in the 6 animals of the third group. The isotopes were injected through a catheter that was introduced into the left humeral artery, the passage of the catheter into that artery being controlled by means of a fluorescent screen; the introduction of the catheter into the renal artery was controlled by means of selective arteriography.

Radioactive isotopes were injected into each dog in a dose of from 8 to 50 mc. In the dogs of the first and second groups, the isotopes remained entirely, or almost entirely, in the injected organ, excluding the danger that might derive from their passage into the general circulation. Some of the isotopes injected into the animals of the third group entered into the general circulation and especially into the reticuloendothelial system of the liver. The isotopes spread themselves uniformly throughout the whole injected kidney in all instances. General reactions were not observed even in instances in which a 50-mc. dose was used. No relevant anatomic damage to the injected kidney was observed in instances in which a small or medium dose (8 to 20 mc.) of Au^{198} or Y^{90} was used. However, degenerative alterations, some of them reversible, of the tubular apparatus and of the glomeruli, inflammation with small cell interstitial infiltration, and circumscribed hemorrhage were observed in instances in which a large dose was used.

In connection with the intra-arterial introduction of radioactive isotopes, no anatomic lesions were found in other parenchymatous organs, and no substantial damage was observed in the arterial tree of the injected kidney, even in instances in which a large dose was introduced. No serious involvement of the kidney function was observed, even in instances in which anatomicopathological examination had revealed a more or less extensive damage to the organ. The author believes that the intra-arterial route, which can be used with no excessive difficulty and with no severe risk for the patient, is worthy of further development and study by clinicians for the radioactive isotope treatment of tumors of the liver, the kidney, and the spleen.

Clinical Trials with Phenethyldiguanide in Selected Patients. R. E. Tranquada, C. R. Kleeman and J. Brown. Am. J. M. Sc. 238:187-192 (Aug.) 1959 [Philadelphia].

This paper is a preliminary report on the results obtained by the use of orally administered phenethyldiguanide (DBI, phenformin) in 32 selected diabetic patients. Selection was based on the severity, the lability, or the etiology of the disease. A successful response to DBI and lowered insulin dosage was noted in 3 of 12 patients with labile diabetes. Four of 8 patients with diabetes secondary to pancreatitis or pancreatectomy were controlled on DBI alone. Control on DBI alone was also obtained in 4 of 10 patients who required high doses of insulin. One of 4 patients who had failed to respond to tolbutamide was successfully controlled on DBI.

The incidence of intolerable side-effects was high. DBI will probably, therefore, be less useful in the therapy of stable adult diabetes than in the treatment of certain other forms of the disease. Its best application may lie in the stabilization of labile diabetes, the regulation of some patients with high insulin requirements, and the management of diabetic patients who are not physically able to give themselves injections. These suggestions are intended only as a guide in the further investigative use of DBI. The authors' conclusions, like those of others, must remain tentative until questions relating to the long-term effect of the drug, i. e., the occurrence of late side-effects, the incidence of diabetic complications, and the longevity of patients treated with DBI for prolonged periods, can be answered by data obtained from the observation of a significantly large group of patients treated for a sufficiently long time.

Gout: Six-Year Follow-Up on Probenecid (Benemid) Therapy. E. C. Bartels and G. S. Matossian. Arthritis & Rheumat. 2:193-202 (June) 1959 [New York].

The authors report on 225 men and 6 women with gout, who were treated with probenecid (Benemid) between 1951 and 1958. The usual age of onset was between 35 and 39 years, and the average duration of the disease before the institution of treatment was 11.4 years. The patients were, on an average, 37.3 lb. (17 kg.) overweight. The number of patients in whom tophi were found increased gradually to reach a maximum of 45% in the 11th year after the initial attack. The average level of serum uric acid for the entire group of patients was 7.67 ± 1.31 mg. per 100 cc. before treatment. Heavy consumers of alcohol tended to have a lower value of serum uric acid, while patients with tophi averaged a significantly higher level. Urinary calculi were passed by 10.5% of the patients, and some form of renal involvement was observed in 27%. A positive family history of gout was obtained in 21% of the patients. Probenecid was given daily in doses of 0.5 to 1 Gm. (500 mg. to patients with nontophaceous gout, and 1 Gm. to those with tophaceous gout). Colchicine in a dose of 0.5 mg. was administered with each 500 mg. of probenecid. Of the 171 patients with adequate follow-up, 153 took probenecid for 12 months, 120 for 2 years, 91 for 3 years, 59 for 4 years, 40 for 5 years, and 20 for 6 years.

The average frequency of acute attacks dropped from 3.6 to less than 1 per year after the second year of treatment. Patients with renal disease showed a smaller drop in serum uric acid level despite large doses of probenecid. Untoward reactions to probenecid occurred in 10% of the patients, one of whom reported transient mental confusion; other patients had gastrointestinal disturbances, such as nausea, heartburn, flatulence, constipation, soreness of gums; a skin rash and definite hives occurred in 7. It is suggested that tophaceous and nontophaceous gout may be 2 clinical varieties rather than stages of a single entity. Renal disease does not necessarily occur in patients with the tophaceous variety of gout, nor is it essential for the development of tophi. Colchicine has been used with probenecid, as it reduces the frequency of acute attacks of gout in the early months of treatment. Great changes in weight are to be avoided until gout is brought under control. Improvement in skeletal changes, reduction of tophi, and a ninefold decrease in frequency of acute attacks were observed in some patients on prolonged therapy with probenecid. All patients who have gout should be offered prolonged therapy with a safe uricosuric agent such as probenecid, since there is no way at present of predicting in which case serious visceral complications may develop.

Steroid Therapy and Vascular Lesions in Rheumatoid Arthritis. R. L. Johnson, C. J. Smyth, G. W. Holt and others. Arthritis & Rheumat. 2:224-249 (June) 1959 [New York].

The authors report 3 cases of malignant rheumatoid arthritis in 2 women, aged 37 and 51 years, and a 63-year-old man who were treated with adrenocortical steroids at 3 hospitals in Denver, and in whom febrile neuropathy and gangrene occurred before death. In each of these patients extensive severe arteritis was found at autopsy. The authors also report clinical observations on 14 outpatients (10 women and 4 men), between the ages of 33 and 73 years, with rheumatoid arthritis in whom peripheral neuropathy occurred during or after administration of adrenocortical steroids, such as cortisone, prednisone, and prednisolone. The findings in these 17 patients support the growing concept that adrenocortical steroids in some unknown manner may activate or accelerate preexisting vascular lesions in patients with rheumatoid arthritis. The neurological symptoms and signs may be the first indication of a disseminated vascular reaction. In each of the 3 fatal cases the polyneuropathy preceded the gangrene, other systemic involvement, and constitutional responses. The pattern of the 14 outpatients was similar but less severe than that of the 3 patients who died, and resembled the neuropathy seen earlier in the 3 patients with autopsy-proved disseminated arteritis. Prolonged high dosage, fluctuations in dosage, or sudden withdrawal of steroids may be followed by chronic hypercortisonism, acute panmesenchymal reactions, or steroid pseudorheumatism. In some patients peripheral neuropathy may occur as a part of these reactions. Ischemic skin lesions, varying from punctate necrosis (on the summit of subcutaneous rheumatoid nodules or in the nail margin) to extensive gangrene, were frequently observed in the patients; these lesions may develop as a part of the diffuse panarteritis.

No specific treatment is known. Prevention of hypercortisonism by sufficiently low steroid dosage and avoidance of fluctuations in dosage and sudden withdrawal of steroid therapy seem important in preventing the occurrence of such vascular lesions. When the initial manifestations of arteritis occur, gradual reduction of steroid dosage may prevent progression of the lesions and ultimately result in amelioration of symptoms and signs. No information seems of specific value in predicting susceptibility of the individual rheumatoid patient to the development of vascular or neural lesions.

Metabolic and Endocrine Studies with Phenethyldiguanide (DBI). T. G. Skillman, F. A. Kruger and G. J. Hamwi. Diabetes 8:274-278 (July-Aug.) 1959 [New York].

A nonsulfonamide hypoglycemic compound, phenformin hydrochloride (or the hydrochloride of phenethyldiguanide [DBI]), was administered orally with meals to 29 diabetic patients. The drug was given for at least 3 days to all subjects and was always continued until a clear-cut appraisal of hypoglycemic response could be made. In all instances fasting blood sugar values exceeded 175 mg. per 100 cc. during the control period despite the administration of a carefully planned diet. In 16 individuals insulin in suboptimal doses also was used during the control period. Fourteen patients met the criteria for adequate hypoglycemic response, while 15 failed to do so. In the responsive group, the fasting blood sugar levels fell from a mean of 240 mg. per 100 cc. during the control period to a mean of 135 mg. per 100 cc. during the 4th, 5th, and 6th days of DBI treatment. None of the patients responding received insulin during the treatment period. In the nonresponsive group, fasting blood sugar levels rose from a mean of 277 mg. per 100 cc. during the control period to an average of 350 mg. per 100 cc. on the 4th, 5th, and 6th days of DBI therapy.

Only 2 young diabetic patients, a 10-year-old girl and a 25-year-old man, were included in the study, and neither responded to the treatment. For the rest of the patients, age correlated poorly with responsiveness. Slightly fewer men than women were studied, but no sex difference was found between those who responded (8 women and 6 men) and those who failed (8 women and 7 men). A high degree of correlation between the duration of diabetes and response to DBI was noted. In the responsive group, the mean duration of diabetes was 1.7 years, and 4 subjects were recently discovered diabetics. No patient who had been diabetic for more than 5 years responded. The mean duration of the disease in the failure group was 8.6 years. No patient who used more than 26 units of insulin responded; the amount of insulin could be diminished 10 to 25% among some subjects classifiable as nonresponsive. Obese patients tended to respond as a group. Variations in daily dosage of DBI from 100 to 300 mg. were necessary to control different patients whose diabetes seemed equally severe.

When blood sugar levels became normal, the customary dose of DBI could be reduced to 150 mg. per day.

Reactions to DBI, other than occasionally encountered generalized weakness, were entirely gastrointestinal and included epigastric discomfort, metallic taste, nausea, vomiting, and frequent defecation. All reactions were transient and regressed promptly with cessation of therapy. DBI in the doses given did not influence thyroid or adrenal function. No evidence of untoward effects upon renal, hepatic, or hematopoietic function was observed during a period of one year's study.

PATHOLOGY

Asian Influenzal Pneumonitis: A Structural and Virologic Analysis. *P. J. Soto, Jr., G. O. Broun and J. P. Wyatt.* Am. J. Med. 27:18-25 (July) 1959 [New York].

The authors report on pathological and virologic studies in 9 patients (5 women and 4 men) with fulminant Asian influenzal pneumonitis which resulted in death. They were seen at the St. Louis University group of hospitals between Sept. 1 and Dec. 1, 1956; their ages ranged from 21 to 54 years. The duration of illness, from the onset of symptoms to death, was from 2 to 15 days. None of these patients had been vaccinated against the Asian strain of the influenza virus. The diagnosis in 6 of the 9 cases was proved by isolation of the Asian strain from the lungs, and in the remaining 3 cases by distinctive histological findings. In all instances the presenting symptoms in the 9 patients were those of the "flu syndrome," characterized by an abrupt onset of fever, sore throat, cough, chills, and myalgia. Rapid deterioration of their condition occurred from the onset of symptoms, with death being due to respiratory or cardiorespiratory insufficiency despite supportive measures, including the administration of antibiotics, cardiac glycosides, oxygen, intermittent positive pressure breathing, and adrenal cortical steroids.

A significant feature in all but 3 of these patients was the existence of an antecedent physiological or an established pathological state. Of the 5 women, 4 were in the later stages of pregnancy or had recently delivered. Other patients had mitral stenosis, myocarditis, myocardial infarction, and Laennec's cirrhosis. It is possible that these conditions had, as a pivotal feature, a functional alteration in vascular hemodynamics; and the structural alterations in the pulmonary vascular bed and air sac resulted in further embarrassment of an already impaired circulatory pathway.

The justified reliance on the efficacy of antimicrobial agents in suppressing bacterial infection allows a clear reappraisal of the nature and lethality of the viral infection. Of the 9 deaths attributed to Asian influenzal pneumonitis, 6 were proved by virologic studies. In 4 of the 6 patients bacteria were cultured from the lungs. Staphylococcus aureus was recovered from 2 patients, anaerobic streptococci from one, and diphtheroids from 2. In the 3 cases in which the virus was not recovered, postmortem procedures precluded the possibility of performing specific diagnostic techniques; a presumptive diagnosis of viral pneumonitis was based on characteristic histopathological features. Anoxemia was thought to be the essential cause of death, the condition being due to a mechanical alveolar-capillary block. Biophysical analysis by ultrasoft x-rays indicated the density of the hyaline membrane, which offered a mechanical block to gaseous exchange. Contributory causes were bacterial superinfection and generalized toxemia.

Cardiovascular Factors in Development of Pulmonary Hyaline Membrane. D. R. Shanklin. A. M. A. Arch. Path. 68:49-57 (July) 1959 [Chicago].

Many theories have been suggested to explain the frequent development of pulmonary hyaline membrane in the prematurely born infant. In most discussions on this problem the emphasis has been placed on pulmonary factors. The author, however, noticed the consistent occurrence of hyaline membrane in infants with interatrial septal defects, and, therefore, suspected cardiovascular factors. For this reason he analyzed the cardiovascular factors and the pulmonary findings in 335 prematurely born infants. All pertinent autopsy material in the files of the department of pathology of Duke Medical Center, Durham, N. C., for 1930-1955 was reviewed. It was found that pulmonary hyaline membrane was significantly commoner in instances of cardiac malformation. The majority of malformations involved circumstances in which the pulmonary vascular bed would be flooded in the presence of what seemed to be a physiologically deficient left ventricle, and 90% of these infants showed hyaline membrane. Several malformations presented opposing circumstances in which this was not likely, and no hyaline membrane was found in these infants.

The incidence of hyaline membrane was increased in infants whose hearts were considered to be hypertrophied. Many factors, including relative ventricular capacities and the possibility of significant postnatal functional patency of the foramen ovale, seem to bear on the adjustments of the neonatal heart. The data obtained in this study suggest that the margin of cardiac reserve in the prematurely born infant, especially with reference to the left ventricle, is less than in the full-term infant, giving rise to an increased incidence of failure and hyaline membrane in the absence of malformations of the heart. The membrane itself is considered to be the end-stage of a progressive development of pulmonary edema fluid, concentration, and precipitation, and loose adherence to the walls of air spaces.

Possibilities and Limitations of Cytohistological Examination of the Sputum by the Fixation Technique in Early Diagnosis of Lung Cancer. W. Montorsi, F. Colombo and A. Peracchia. Minerva med. 50:1673-1693 (May 30) 1959 (In Italian) [Turin, Italy].

Cytological study of the sputum of 146 hospitalized patients with suspected lung cancer was made by fixation in paraffin, sectioning, and staining with hematoxylin and eosin. Malignancy was demonstrated by histological examination in 66 patients. False-negative diagnosis by cytological examination was made in 9 patients. This could be attributed to the presence of adenocarcinoma in 5 patients, the cells of which are found infrequently in the sputum, and to either the peripheral location of the tumor or the absence of communication between the tumor and the bronchial tree in 4. The examination was made in one patient 3 times, and positive reaction for lung cancer was established only on the third examination. False-positive diagnosis by cytological examination was made in one patient. The error was attributed to a mishap whereby, by mistake, material obtained from another patient was examined. Both biopsy and cytological findings were positive for lung cancer in 24 patients, and negative in 7. A positive biopsy and a negative cytological finding resulted in 2 patients, whereas negative biopsy and positive cytological findings resulted in 33. False-negative and false-positive diagnoses in cytological examination of the sputum by the fixation method in early detection of lung cancer are limiting, but not excluding, factors. This procedure deserves further improvement and application.

Diagnostic Cortical Biopsy: A Histological and Chemical Study. W. Blackwood and J. N. Cumings. Lancet 2:23-24 (July 11) 1959 [London].

The authors report the results of histological and chemical examination of small pieces of cerebral tissue removed at biopsy from 65 patients with progressive dementia. The biopsy specimens were taken from a presumably diseased cerebral hemisphere and usually from the frontal lobe. A single cube of tissue, with sides at least 1.5 cm. long, including white and gray matter, was removed through a 3.15-cm. trephine hole and forwarded to the laboratory with all speed. In the laboratory the specimen was divided into 2 parts; one part was fixed in 10% formol-saline and examined histologically, while the other was examined chemically. The age and the main clinical features of each patient were made known, and independent diagnoses were made. The histological diagnosis of the lesions found was based on well-recognized features previously described by Greenfield and associates. The chemical examinations included estimations of total phospholipids, total and esterified cholesterol, hexosamine, neuraminic acid, and water content. In 36 of the 65 biopsies, a positive diagnosis by one or both methods of examination could be made. Findings in 23 biopsies revealed no abnormality, either histologically or chemically. In some cases the histological and chemical examinations were in agreement; in others only one method was diagnostic. The different methods gave apparently conflicting diagnoses only once. These findings show that in 3 biopsies out of every 4, in which some abnormality was present, a positive diagnosis was possible by a combined chemical and histological approach. It is emphasized that any new approach which aids diagnosis and is not injurious to the patient is valuable.

Psammoma Bodies and Thyroid Cancer. G. H. Klinck and T. Winship. Cancer 12:656-662 (July-Aug.) 1959 [Philadelphia].

The authors examined thyroid tissue from a total of 2,626 patients (children and adults) in order to determine the diagnostic significance of psammoma bodies in the thyroid and to find out whether they occur in conditions other than carcinoma. The average age of the adults was 41 years and that of the children, 9 years. The material included 470 specimens from cases of primary thyroid cancer, 3 from cases in which the diagnosis of cancer was in doubt; 132 were cases of "chronic thyroiditis," and 28 cases in which the thyroid contained a metastatic carcinoma. The remaining specimens were from nontoxic goiters, toxic goiters, and essentially normal thyroid glands and also included a variety of adenomas.

Psammoma bodies were found with equal frequency in the 2 sexes but more commonly in children than in adults. They were found in 48% of primary thyroid tumors (including 3 in which the diagnosis of cancer was equivocal) but in only 1 of 2,153 noncancerous thyroids. Twenty-one per cent of the patients with primary cancer in the vicinity of the thyroid showed psammoma bodies in their thyroids, which were otherwise normal. This indicates that search for carcinoma must be instituted when such bodies are found in noncancerous thyroids.

Study of the material in this series suggests that psammoma bodies occur at the site of degenerating or dead epithelium. Psammoma bodies in thyroid or in lymph nodes unassociated with epithelium presumably mark the site previously occupied by metastatic cancer cells that failed to survive.

BOOK REVIEWS

Health Insurance. By O. D. Dickerson, Ph.D., C.L.U., C.P.C.U. Irwin series in insurance. Editors: Edison L. Bowers and Davis W. Gregg. Cloth. $6. Pp. 500, with illustrations. Richard D. Irwin, Inc., Homewood, Ill., 1959.

This book is the result of a great deal of research on the broad subject of health insurance. It is divided into four general sections, with the following captions: Health Losses and How They Are Met; Expense Coverages; Income Coverages; and Health Insurer Operations. Of necessity, the text treats a wide range of topics in order to give the reader a better understanding of what has occurred in the past 20 years in a rather heterogeneous development which is now a major force in health economics. In addition to a discussion of health insurance, as the term is now generally interpreted, there also are discussions of several phases of social insurance, including workmen's compensation, nonoccupational disability laws, and old-age, survivors, and disability insurance. It also makes brief mention of public assistance programs. Blue Shield, Blue Cross, insurance companies, and other organizations involved in the broad field of health insurance are discussed. As a result of his studies the author concludes that there are perhaps more differences among programs within the same category of plan than there are between the various categories of plans.

The general types of benefits offered by companies and plans are outlined, and the author explains many of the administrative phases of health insurance, such as underwriting, rate-making, the different classes of reserves, claims processing, and regulation by state insurance supervisory authorities. In addition to describing the various programs in existence, the author comments on their similarities, differences, and in some instances on their interrelationships. He predicts that the pattern of health insurance in the future may involve either "major-medical" or "comprehensive" coverage, both of which are of relatively recent origin.

The book contains 31 tables, 5 appendixes, and a general bibliography. In addition, selected references on specific topics are listed at the end of each chapter. Each chapter has a summary. In 9 of the 19 chapters there is also a separate section entitled Problems and Issues, wherein the author brings differing opinions into focus. The book is well indexed. This publication is a single source of valuable information for many who are interested in health insurance, and it is suitable for a college level textbook. It should be of interest to physicians and others who wish to have more than a superficial knowledge of the many ramifications of health insurance and related matters.

Basic Physics in Radiology. By L. A. W. Kemp, B.Sc., Ph.D., F.Inst.P., *Chief Physicist to London Hospital*, London, and R. Oliver, M.Sc., F.Inst.P., A.M.I.E.E., Principal Physicist in Department of Radiotherapy of United Oxford Hospitals, Oxford. Cloth. $8.50. Pp. 329, with 143 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

This book discusses the principles of basic physics which are likely to find application in the field of radiology. It does not cover the field generally known as radiologic physics. After single short chapters on statics, dynamics, and heat the authors discuss the various aspects of magnetism and electricity. The subject matter is presented in a straightforward and lucid fashion. There is no discussion of optics, which would seem to be within the scope of such a textbook. This volume will find only limited use in medical fields.

Dermatologie und Venereologie, einschliesslich Berufskrankheiten, dermatologischer Kosmetik und Andrologie. In fünf Bänden. Herausgegeben von Prof. Dr. Dr.h.c. H. A. Gottron, Direktor der Universitäts-Hautklinik Tübingen, und em. o.ö. Prof. Dr. Dr.h.c. W. Schönfeld. **Band III/Teil 1: Hautveränderungen durch äussere Einwirkung: Allergische Krankheiten und toxische Schädigungen der haut Formenkreis des Ekzems.** Bearbeitet von C. Böhm et al. Cloth. 165 marks, $39.30; subscription price 132 marks, $31.45. Pp. 695, with 232 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

This is the first of two sections of the third volume of a five-volume German encyclopedia on dermatology and venereal diseases. This issue alone lists 22 contributors from various German and Austrian dermatological centers. In it the effects of external influences on the skin and allergic and toxic manifestations, including eczema, are covered in detail. The first section deals with thermal and electrical burns and the effects produced by acute and chronic exposure to cold. Electrical and chemical burns are discussed, but the damaging effects of ionizing radiation are omitted. The effects of light on the skin, and diseases caused by light, including porphyria, are presented in an interesting and comprehensive manner. There is a chapter on dieases of the peripheral blood vessels, including acrocyanosis, livedo, Raynaud's disease, and the forms of angiitis.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

In the chapter on varicose veins and phlebitis ,the conservative forms of treatment are emphasized, including conventional means of control by bandaging and sclerosing injections, whereas surgical treatment is minimized. There is a chapter on anal diseases, including pruritus, anal fissure, and hemorrhoids, which tends to encompass more than lies within the usual province of the dermatologist. The discussion of allergic manifestations and toxicodermas includes two excellent chapters on diseases caused by plants and drug eruptions and a comprehensive summary of present knowledge of immune biology of the skin. The discussion of eczema is divided into chapters on contact dermatitis, eczema vulgaris, endogenous eczema (atopic dermatitis and prurigo), lichen Vidal, and seborrhea. There is also a brief discussion of occupational dermatoses and the influence of trauma on diseases of the skin.

At the end of each chapter is an exhaustive, and often exhausting, bibliography. The section on contact dermatitis, including less than 50 pages of text, has more than 14 pages of references alone. Few of the references are of later date than 1956. There are a few small color plates, but the numerous black and white illustrations are all excellent. Unfortunately, the system of numbering the illustrations is not consecutive throughout the volume. The text and format of the volume are excellent. This work can be recommended as a valuable source of reference for specialists in this field and for libraries, but the coverage is probably too comprehensive for everyday use by the general practitioner.

The Mast Cells. By James F. Riley, M.B., Ch.B., M.D. Foreword by Sir Henry Dale, O.M., G.B.E., F.R.C.P. Cloth. $6.75. Pp. 182, with 65 illustrations Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 & 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

The author of this monograph is a recognized authority on mast cells. Ever since their discovery by Ehrlich in 1877, a great deal has been written about these puzzling cells. Little new was added, however, until 1937, when Holmgren and Wilander showed that mast cells are the site of formation or storage of heparin, the natural anticoagulant of circulating blood. The next major contribution came from the author of this monograph, who brought forth impressive evidence that mast cells produce histamine.

The book consists of two main parts. The first is a review of the growth of our knowledge of mast cells, and the second is derived from the author's original investigations. His hypothesis of the origin of histamine in mast cells is convincingly supported by experimental evidence. The role played by mast cells in the skin of animals treated with carcinogenic agents is interesting. Those interested in the action of histamine and in mast cells should enjoy this excellently written and well-indexed monograph. The bibliography is all inclusive.

Educators may be interested in the circumstance that determined the author's decision to devote himself to the study of mast cells. One of his favorite teachers discussed his own observations on carcinogenesis and called attention of his students to mast cells in the skin of mice treated with tar. When asked by a student what was the function of these cells, he replied that he did not know. This confession of ignorance on the part of a favorite teacher was responsible for the decision of the author to devote himself to this subject. The results show that a teacher who has the courage to admit ignorance to his students may make a real contribution to their future intellectual and scientific development.

Ciba Foundation Symposium on Amino Acids and Peptides with Antimetabolic Activity. Editors for Ciba Foundation: G. E. W. Wolstenholme, *O.B.E.*, M.A., M.D., and Cecilia M. O'Connor, B.Sc. Cloth. $8.75. Pp. 286, *with 28 illustrations*. Little, Brown & Company, 34 Beacon St., Boston, 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London W. 1, England, 1958.

This is another in the series of Ciba Foundation symposiums. The subject matter ranges from the stereochemistry of naturally occurring B-amino acids through the influence of amino acid deficiencies on experimental cancer chemotherapy and the mode of action of chloramphenicol. The volume should appeal mainly to organic chemists and biochemists who are interested in the reactions, characterization, and synthesis of organic compounds containing amino acids and having chemotherapeutic value. Almost two-thirds of the book is devoted to the chemistry of such substances. Among the compounds discussed, besides those mentioned elsewhere, are actinomycin, etamycin, cyclic polypeptides, and bacitracin. It should also appeal to experimenters in the field of cancer chemotherapy for its excellent discussions of the antitumor activity of azaserine and nitrogen mustard derivatives of amino acids.

Although the book contains only a few sections of direct interest to the clinician, the three chapters dealing with clinical trials with azaserine and related compounds, with nitrogen mustard derivatives of the amino acids, and with the actinomycins provide an excellent summary of the use and limitations of these compounds in cancer chemotherapy. The discussions following these chapters are stimulating and can be read with profit by anyone having even the slightest interest in chemotherapy. The basic problem of chemotherapy, that of relating structure to biological function, is appraised particularly well in the comments following the papers on azaserine and related compounds by Christine Reilly and J. M. Buchanan, and the goals of chemotherapeutic research are pinpointed. Although this is a book for the specialist, the nonspecialist who dips into it selectively will do so to his advantage.

QUESTIONS AND ANSWERS

UTERINE RETROFLEXION AND PAIN

To the Editor:—*A 29-year-old woman has almost continuous pain and soreness in the lower part of her abdomen which is increased during menstruation. Pelvic examination indicates a retroverted and retroflexed uterus which is apparently incarcerated in this position. Would the abnormal position of the uterus cause the pain? Is an operation indicated to bring the uterus to its normal position?* *M.D., New York.*

Answer.—Uncomplicated uterine retrodisplacements rarely cause lower abdominal discomfort. Endometriosis involving the adnexa, the sacroiliac ligaments, and the cul-de-sac can result in fixation of the reproductive organs in the sacral cavity. Discomfort is usually limited to increasing dysmenorrhea and pain on coitus. Residual pelvic inflammatory disease can cause lower abdominal pain and soreness. Enlarged polycystic ovaries may be positioned behind the uterus, but they can be moved by palpation and are often associated with disturbed menstrual function.

Uterine suspension to correct retrodisplacements is rarely indicated. Diagnostic studies should be completed for organic disease of pelvic organs. Psychosomatic factors can cause lower abdominal discomfort and should not be overlooked. An exploratory operation can be considered if pelvic inflammatory disease or endometriosis is the likely cause.

ENDOMETRIOSIS

To the Editor:—*What is the conservative management of endometriosis in a 30-year-old woman who has two children and desires more children later? Is suppression of menstruation with testosterone or diethylstilbestrol advisable? Would excision of a small endometrial cyst in the right adnexal area be indicated, even though there has been no enlargement in five years?*

Frank L. Groat, M.D., Grand Haven, Mich.

Answer.—Endocrine therapy may be used in the conservative management of endometriosis in a woman who wishes to have her reproductive functions preserved. Suppression of menstruation may be accomplished with androgen, estrogen, or estrogen with progesterone. Estrogen may be given in the form of diethylstilbestrol, 1 mg. three times daily, and increased every five days as follows: 2, 3, 5, 10, 15, and 25 mg. three times daily. Should bleeding ensue, the dosage of diethylstilbestrol may be increased to as much as 100 mg. three times daily, for a period of three months. Side-effects of diethylstilbestrol therapy are nausea, vomiting, breast engorgement, vaginal bleeding, and severe leukorrhea. Androgen may be given orally or sublingually in doses of 5 to 10 mg. of methyltestosterone daily for three months. Testosterone propionate may be given parenterally; the amount given per month should not exceed 200 mg. Side-effects of testosterone therapy include acne, hirsutism, deepening of the voice, and atrophy of the labia and vagina. Patients must be warned about these side-effects and treatment discontinued when they appear. The hirsutism and voice changes may persist after therapy is discontinued.

Dr. R. W. Kistner has reported the use of newer progestogens in the treatment of endometriosis (*Am. J. Obst. & Gynec.* 75:264 [Feb.] 1958). The treatment is based on the fact that pregnancy itself improves endometriosis; a pseudopregnant status can be produced with use of 17-alphahydroxyprogesterone caproate, with estrogen, norethynodrel, or norethindrone. A combination of progestational and estrogenic substances in large, continuing doses produces amenorrhea and a decidual reaction in the endometrium. At the end of therapy the patient has withdrawal bleeding, which is usually minimal, and the extrusion of an endometrial cast of the uterus.

Operative treatment, in a patient aged 30, should be conservative. It would be indicated if endocrine therapy was of no, or only temporary, benefit. If the nature of the cyst were in doubt excision would be indicated. The diagnosis of pelvic endometriosis is always in doubt, short of visual evidence obtained by culdoscopy or laparotomy.

RODENT POISON

To the Editor:—*What are the symptoms of poisoning by compound 1080? Should the meat of an animal dying from it be eaten?*

Myra Babcock, M.D., Pleasant Ridge, Mich.

Answer.—Sodium fluoroacetate (compound 1080) is a synthetic, water-soluble, nonvolatile salt, with a faint odor like that of vinegar. As an experimental rodenticide it has no equal in terms of potency, stability, and acceptability in rodent baits and drinking water. This substance is not available to

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

the general public and should be used only by professional exterminators and other experts, because of its high toxicity for mammals. The mean lethal dose in man is between 1 and 5 mg. per kilogram of body weight. In the body it forms fluorotricarboxylic acid, which blocks cellular metabolism at the citrate stage. The relationship between this metabolic effect and poisoning has not been elucidated. All body cells, and especially those of the central nervous system, are affected by fluoroacetate.

The principal manifestations of fluoroacetate poisoning are vomiting and convulsions. Symptoms in acute poisoning (from ingestion or inhalation) begin at any time up to four or five hours, with vomiting, excitability, tonic-clonic convulsions, irregularity of heartbeat and respiration, exhaustion, coma, and respiratory depression. Death is from respiratory failure and paralysis of the heart and central nervous system. Chronic poisoning has not been reported. Experimental studies indicate that a dose less than that necessary to produce acute symptoms produces no effect. Justus C. Ward, of the U. S. Department of Agriculture, (*Pest Control* 26:14-16 [Jan.] 1958) comments on the problem of secondary poisoning: "Since the amount of [compound] 1080 left in the dried carcass of a single rat often can kill a dog, the necessity for prompt recovery of a dead or dying rodent is apparent."

MALODOROUS URINE

To the Editor:—*A 34-year-old married woman has complained of malodorous urine for four years. This has been confirmed by her husband and children. It has been present daily and is not related to her menses or to coitus. The only time that it was not evident was when she was hospitalized for treatment of pulmonary tuberculosis, a period of seven months. Genitourinary tract examinations and a urine culture gave negative results. The catheterized urine specimen had no odor. What is the cause of this odor?*

M.D., Michigan.

Answer.—An offensive odor after urination is perplexing, and an explanation for it often elusive. When the odor is detected by others, it is not likely that "patient hyperesthesia" is the cause of the complaint. Odors are usually due to infection, but they may be caused by an excess of body oils, which would appear with certain phases of the menstrual cycle and then become rancid. The odor may be secondary to cervicitis, vaginitis, bartholinitis, skenitis, or urethritis. The absence of odor in the catheterized urine would indicate that its origin is not in the upper urinary tract. Muscle movements during micturition would force foul-smelling material from the urethra or the genital tract. The absence of odor during the time the patient was treated for tuberculosis could indicate that the causative organism was affected by streptomycin, which the patient may have been receiving at the time. A search for chronic infection in the areas mentioned should be made and bacterial culture studies done. Treatment would depend on the findings.

CONTROL OF EXCESSIVE GROWTH

To the Editor:—*Is there any practical and safe management to inhibit the growth factor to slow the height development of a girl 13 years old?*

Paul J. Bronson, M.D., Terre Haute, Ind.

Answer.—To verify the diagnosis of increased growth hormone one should make a roentgenogram of the sella turcica, determine the 24-hour output of 17-ketosteroids and total corticoids in the urine, make an eosinophil count, do a glucose tolerance test, and determine the basal metabolic rate or protein-bound iodine or radioiodine uptake, depending on the availability of these tests. If there is no abnormality of adrenal function and no hyperthyroidism, the girl should be given thyroid to tolerance, beginning with 60 mg. per day and increasing by 15 mg. per day at weekly intervals until tolerance is determined. Therapy should be continued at that level. She should also take 0.02 mg. of ethinyl estradiol once a day three weeks out of four. This program should be continued for three months. If there is no increase in height by that time, this regimen can be continued. If she shows increased growth, the pituitary can be irradiated. If there is an enlarged sella turcica, the pituitary should be irradiated prior to drug therapy. There is a description of this procedure by Lisser (Gigantism and Acromegaly, in Postgraduate Course in Endocrinology presented by Association for Study of Internal Secretions, Feb. 23-28, 1948, Los Angeles, compiled by Hollywood Reporting Service, 1121 Vine St., Hollywood 38, Calif.).

PREVENTION OF DUODENAL ULCER

To the Editor:—*What preventive measures should be ordered for a patient who has recently recovered from a duodenal ulcer and must take steroid preparations for the treatment of joint disease?* *Marks S. Shaine, M.D., New York.*

Answer.—The only currently known methods of preventing the recurrence of duodenal ulcer in patients receiving steroid therapy are (1) the use of antacids with doses of steroids between meals and at bedtime, and appropriate use of antiulcer diet and drugs, and (2) the use of the smallest possible daily doses of steroids at all times, keeping doses within the usual limits of tolerance of patients for long-term administration. Reactions to overdosage are much more likely to be encountered if administration is continued beyond a few weeks or if doses are in excess of about 9 mg. of prednisone (or comparable doses of other steroids) per day for a man. (Women, especially in the postmenopausal age group, generally have lower levels of tolerance for long-term administration of adrenocortical steroids.)

Steroid therapy may not be advisable if (1) the prospects of complications therefrom exceed the likelihood of beneficial effects; (2) other therapy will be adequate; or (3) long-term administration is required, and the results from doses of steroids within each patient's anticipated range of tolerance are not satisfactory.

POLLUTION OF RIVER WATER

To the Editor:—*Can the origin of river contamination be determined by the type of bacteria found in the water? Would changes of bacterial flora along a 30-mile portion of the river indicate the place of contamination?*

Benjamin L. Yellen, M.D., Brawley, Calif.

Answer.—The coliform group is accepted as the bacteria which indicates fecal pollution. Unpublished data from the Robert A. Taft Sanitary Engineering Center indicate that the strains of coliform bacteria from human pollution and those from cattle, pigs, sheep, and tame ducks are similar. There are no practical methods for distinguishing the fecal coliforms derived from human excreta from those from other animal feces. Streptococcus faecalis biotype fecium (S. fecium "Orla-Jensen") is the dominant species in pigs (Ingram, M., and Barnes, E. M.: *Ann. Inst. Pasteur, Lille* 7:115-119, 1955). A report by Cooper and Ramadan (*J. Gen. Microbiol.* 12:180-190 [April] 1955) suggests that it might be possible to distinguish human from animal pollution by a carefully devised test for fecal streptococci, since S. bovis is definitely of animal origin and absent from the human intestine. S. faecalis is the dominant strain in human feces. The method for species separation is cumbersome, and there is not sufficient data to interpret the results quantitatively, in relation to the sources of pollution of river water.

FIRST AID FOR PROSPECTORS

To the Editor:—*What drugs and medical supplies should be taken on a prospecting trip to the mountains of Honduras? There will be three to five people in the group, and there will not be a physician with them.*

F. R. Peterson, M.D., Butte, Mont.

Answer.—Travelers to Honduras should be vaccinated against yellow fever, smallpox, typhoid, and tetanus. Certificates of smallpox vaccination are required of all arrivals in Honduras, and evidence of recent smallpox and perhaps yellow fever vaccination is required for reentry into the United States. A first-aid kit, containing such drugs as aspirin, and sterile bandages would be necessary, as well as chloroquine for suppression of malaria, in 0.5-Gm. doses or 2 tablets once a week on the same day each week, for when the presence or absence of malaria is not known in a country, this drug should be started on entry. A supply of one or two broad-spectrum antibiotics should be included. Kaolin and pectin would be used for controlling diarrhea. Chlorine disinfectant tablets are recommended for sterilization of drinking water, when water cannot be boiled. The physician should be sure that a patient going to isolated areas can tolerate the drugs recommended for emergency or long-term use. "Health Hints for the Tropics" is a book for travelers, which may be obtained for 25 cents from the National Institutes of Health, Bethesda 14, Md.

INTERMITTENT TRACTION

To the Editor:—*Are intermittent traction devices proper instruments for treating patients with injuries (fractures, dislocations, or sprains) of the spine?*

Delbert L. Warwick, M.D., Costa Mesa, Calif.

Answer.—Intermittent traction devices may be used to provide traction on the cervical or lumbar spine for the treatment of arthritis and intervertebral disk injuries, with narrowing of the intervertebral disk spaces, and certain types of nerve root compression. There is no type of fracture for which the intermittent traction would be of value. Acute paravertebral muscle sprains are treated by rest and muscle relaxants. Continual flexion traction is usually more effective than intermittent traction. Most devices apply traction force to the neck in a line parallel to the long axis of the body. This may relieve pressure on nerve roots in some instances, but the intervertebral foramens through which the nerve roots emerge enlarge when the neck is flexed, and traction with the neck in this position is more likely to relieve pressure on the nerve root. Pelvic traction with the patient in the Williams position (flexion of the spine, hips, and knees) is better than straight traction. No intermittent traction device on the market is suitable for providing flexion as well as direct traction.

ALLERGY TO TICK VACCINE

To the Editor:—*A 42-year-old man received two injections of Rocky Mountain spotted fever vaccine (egg embryo commercial type). Immediately after each injection he had painless hematuria, lasting for 24 to 48 hours, and no cause for the hematuria was found. Could this be a reaction to the vaccine? Should the third injection be given?*

T. A. Morgan, M.D., Franklin, Va.

Answer.—If the painless hematuria was a reaction to the vaccine, it would be due to either the egg or the rickettsial protein. No such reaction has been known to follow injections with rickettsial vaccine, and, if it were, it would have been a delayed rather than an immediate reaction. If this were an allergic reaction it would be due to the egg protein. Allergic reactions to egg have occurred with similar vaccines prepared from the egg embryo. These have usually been of the urticarial type or have precipitated attacks of asthma in an asthmatic patient. Whether this was an allergic reaction to egg or to some other antigen, it would be inadvisable to give the patient a third injection of the vaccine, because it might provoke another, more severe, attack of hematuria. If the patient should become infected with the rickettsial organism, such infections are amenable to treatment with our present antibiotics.

ENDEMIC DISEASES OF PUERTO RICO

To THE EDITOR:—*What diseases are endemic to Puerto Rico and what public health problems are likely to be encountered there? Are there any special considerations that an examiner should be aware of in performing preemployment physical examinations?*

Edward J. Zebrowski, M.D., Plainville, Conn.

ANSWER.—Diseases endemic to Puerto Rico include those of parasitic origin that are common in the United States, with amebiasis being the most important. The intestinal helminthiases, principally Ascaris, Trichuris, and hookworm infections, are most prevalent in rural areas. Schistosomiasis is indigenous to Puerto Rico, where it is of considerable public health and economic importance. Shigellosis is a common infection and often a cause of death for infants and debilitated older persons. Fungus diseases of the skin and middle ear are frequent in this semitropical climate.

Physical examinations for employment should be thorough and accompanied by a comprehensive history. The type of work to be performed and anticipated exposure to toxic materials may require clinicolaboratory tests, including liver and kidney function tests, since the infectious diseases of this climate cause hepatic and renal damage.

INVERSION OF APPENDICEAL STUMP

To THE EDITOR:—*What are the contraindications for inverting the appendiceal stump as the technique in an appendectomy?*

W. C. Schwartz, M.D., Manhattan, Kan.

ANSWER.—The appendiceal stump may or may not be inverted, and there are no statistics which indicate that one method is better than the other. It is best not to invert the stump when the base of the appendix is indurated, because this may make inversion difficult and allow the sutures to tear out. If not inverted the stump should be treated with a caustic (phenol) and may be covered with a tag of fat, omentum, or mesoappendix. The appendiceal aperture is small, and simple ligation has proved to be satisfactory. Inversion usually is not done when there is an abscess close to the inverted stump, for there may be interference with the blood supply and subsequent tumefaction at the site of inversion. If the stump is inverted, in this circumstance, an absorbable suture should be used; the inversion is just enough to bury the stump and the purse-string suture should be carefully placed. The experienced surgeon will select the technique he judges the best for each situation.

SYMPTOMS OF AGING

To THE EDITOR:—*A 70-year-old woman has complained of a burning sensation in her mouth, throat, and tongue. She lives alone and has few outside interests. In the winter months her daughter visits her, and during this time she complains less frequently. She has a cataract of the right eye and pain in the right temporal region. Her home is heated by an open gas burner which is in the living room and has no outside flue. She feels cold most of the time, and the gas burner is on almost continuously.*

Byron W. Gutheil, M.D., Pasadena, Calif.

ANSWER.—This patient complains of symptoms commonly observed in elderly persons. The pain in the temporal region may be due to neuritis of the sympathetic ganglions of the head or neck and the ninth nerve. Proper ventilation of the house is well advised, although sensitivity to cold is common in elderly persons. The decrease of symptoms when her daughter visits her indicates the emotional component of the problem. Treatment would include improvement of diet, more effective heating and ventilation of the house, and an attempt to make her live a more active, less reclusive life.

TINNITUS

To THE EDITOR:—*A 55-year-old man complains of pounding in the ears when he is lying down. Eye fundi appear normal for his age, blood pressure has varied from 162/84 to 140/90 mm. Hg, and he shows no signs of peripheral arteriosclerosis. There is slight rounding of the left ventricle on fluoroscopic examination. He has no other signs of cardiac disease, and the physical examination was otherwise normal. What is the cause and treatment for the sensation of pounding in the ear?*

M.D., West Virginia.

ANSWER.—The cardiovascular system is often responsible for various types of tinnitus, including pounding. Patients will sometimes both feel and hear their pulse in the ear when it becomes accentuated due to changes in pressure. Cardiovascular pathology, such as valvular lesions, arteriovenous aneurysm, and anemia, can produce tinnitus, and cranial vascular anatomic variations may also account for this symptom. In view of the patient's history, use of a tranquilizing drug for a short period of time is suggested.

MARRIAGE OF THIRD COUSINS

To the Editor:—*A young couple was anticipating marriage until they found that their great-grandfathers were brothers. Should they stop seeing each other because of the distant relationship? They are college graduates, emotionally stable, and in good health. The girl's mother is a "neurotic" person, but there have been no physical abnormalities or serious mental disturbances in either family.*

Theodore Hirsch, M.D., Newark, N. J.

Answer.—The young man and woman are third cousins; thus, a part of their genetic ancestry is common to both, and recessive defects might become evident in their progeny. Recent study of the effects of radiation, either from explosions or from natural sources, shows that the number of these recessive defects is greater than has previously been calculated. Since the two persons here concerned are only third cousins, and their ancestry is normal as far as known, the cause for anxiety is certainly not great. If the marriage seems desirable in every other way, the fact of this distant relationship is hardly worth forcing a change in their future.

ENDOMETRIAL CYST

To the Editor:—*A 23-year-old single woman has, for the past two years, had a nodular swelling in the right inguinal area. It would appear 10 to 14 days prior to the menses and subside with the menstrual flow. It would develop to about 2 cm. in diameter, was tender, and seemed to be in the skin or subcutaneous tissue. During the last six to nine months her periods have been two or three weeks later than usual, and the nodule now appears with menstruation. Is the nodule related to the menstrual cycle? Should it be excised? What treatment is indicated?*

M.D., Michigan.

Answer.—This nodule is connected with the menstrual cycle and may be endometriosis, even though the location is most unusual. It should be removed surgically and studied microscopically.

PREGNANCY AND PEPTIC ULCER

To the Editor:—*What is the frequency of peptic ulcer during pregnancy and the postpartum period?* *Morris H. Levine, M.D., Denver.*

Answer.—In a review on peptic ulcer and pregnancy Vasicka, Lin, and Bright (*Obst. & Gynec. Surv.* 12:1 [Feb.] 1957) stated that the incidence and frequency of peptic ulcer during pregnancy are more or less conjectural, because peptic ulcer may be asymptomatic or the symptoms may be erroneously attributed to usual ptyalism, hyperemesis gravidarum, anemia, epigastric pain, or other signs and symptoms of pregnancy. There are few reports of gastrointestinal hemorrhage from peptic ulcer during pregnancy. The literature available is concerned with patients in whom the outcome was fatal, and there are not many. Perforation or hemorrhage of peptic ulcer commonly occurs during the last trimester, during labor, or in the immediate postpartum period. Johnston (*Obst. & Gynec.* 2:290 [Sept.] 1953) added 2 cases of death from peptic ulcer in pregnancy to the 15 previously reported in the literature.

DIARRHEA DUE TO GASTROJEJUNOSTOMY

To the Editor:—*A posterior gastrojejunostomy was performed on a 74-year-old man who has carcinoma of the stomach. His postoperative recovery was good, but two months after the operation he began to have diarrhea which was mostly passage of water. His appetite has been good, but in spite of a normal food intake he has lost weight for seven months. Could there be a causal relationship between the gastrojejunostomy and the diarrhea?*

F. X. Van Lieshout, M.D., Little Chute, Wis.

Answer.—The most likely cause would be a gastrojejunocolic fistula which developed in the two months after the gastrojejunal anastomosis. It should be visualized by means of a barium enema, and repeated stool examinations should reveal the presence of occult blood from the gastric carcinoma. Frequent watery stools can be due to achlorhydria, which is often present with carcinoma of the stomach. Carcinomatosis of the perineum could cause hyperistalsis, which in turn would cause water-laden diarrhea.

PIGMENTED PERSPIRATION

To the Editor:—*A 24-year-old woman had skin lesions which appeared in the third month of her second pregnancy. The straw-colored spots were 0.5 cc. in diameter, irregular in shape, appeared on the upper chest wall, and stained the patient's clothing. This condition was also present during the first pregnancy and had occurred when she was in her teens. What is the diagnosis?*

Paul T. C. Chen, M.D., Accokeek, Md.

Answer.—Localized chromhidrosis would be the most likely diagnosis. In this condition colored sweat is produced by ectopic apocrine glands. The lesions usually occur on the face but may be present on the chest and abdomen. The color is most often blue or black, but a yellow or straw-colored secretion may occur. Microscopic examination of the apocrine glands shows increased pigment, which may be a type of lipofuchsin. The pigmented secretions may be eliminated for short periods by mechanical stimulation, local heat, or adrenergic stimuli, but the treatment is not satisfactory.

LEUKEMIA AND MENORRHAGIA

To the Editor:—*What would be the best method of preventing excessive blood loss by the increased menstrual flow of a young woman who is ill with acute myelogenous leukemia?*

Lester Lando, M.D., Monsey, N. Y.

Answer.—The control of uterine bleeding in a patient who has acute myelogenous leukemia should take into consideration the gravity of the disease, the response to therapy, and the hemorrhagic manifestation of the disease. Life expectancy is about six months; thus, major operations are rarely indicated. Artificial menopause induced by irradiation of the ovaries is probably the least hazardous procedure. Curettage is usually ineffective in the control of bleeding of systemic origin. The suppression of ovulation by the newer progestational agents is not likely to control uterine bleeding. Major operations are tolerated poorly by patients with myelogenous leukemia and should be performed only as a last resort.

CARCINOMA IN SITU DURING PREGNANCY

To the Editor:—*What is the treatment of carcinoma in situ of the cervix in a 34-year-old woman who is three months pregnant?*

M.D., New York.

Answer.—If the diagnosis was suspected because of vaginal cytological examination, then multiple quadrant biopsy or cone biopsy should be performed to confirm the diagnosis, since cytological evidence alone is not sufficient. If the biopsy specimen contains the entire in situ structure, then no further therapy is indicated at this time. Smears should be repeated throughout the pregnancy to assure that the lesion has been removed and does not recur. Delivery should be anticipated to be normal through the birth canal. If smears should be positive at any time, then another biopsy must be done; and if recurrence is demonstrated, hysterectomy is indicated.

ACRODERMATITIS CONTINUA

To the Editor:—*What is the treatment for acrodermatitis continua?*

Howard M. Cooper, M.D., Rutherford, N. J.

Answer.—Acrodermatitis continua of Hallopeau (also known as acrodermatitis perstans or dermatitis repens) is a chronic bacterial dermatitis. It is an infection of the paronychial tissue which starts on the fingers and may extend to involve the entire extremity and occasionally the trunk. Excision of the infected area and skin grafting would be contraindicated, because the infection may persist and extend beyond the grafted areas. The infecting organisms are Staphylococcus aureus and Pseudomonas aeruginosa, and the administration of appropriate antibiotics both internally and locally is the preferred treatment.

DOLICHOCEPHALY

To the Editor:—*Four years ago a patient who had rubella (German measles) in the first trimester of her pregnancy delivered an infant that was normal except for dolichocephaly (long-headedness). His growth and development were normal, and the abnormal shape of the head has been corrected. The mother has divorced the boy's father and remarried. Was the dolichocephaly caused by the rubella? Is the anomaly likely to be repeated in children of the new marriage?*

O. Hunter McClung Jr., M.D., Lexington, Va.

Answer.—The cranial abnormality of this child did not result from the maternal rubella. The condition is not genetically determined and should not appear in any subsequent offspring of this mother. The probability of the abnormality appearing in another child is decreased further by the fact that she is now married to another man.

DRUGS IN DONOR BLOOD

To the Editor:—*What limitations should there be on the use of blood from donors who are taking psychochemical drugs?*

Martin H. Weinberg, M.D., Hammonton, N. J.

Answer.—Blood from donors who are taking psychochemical drugs is safe for administration to almost all recipients. The amount of the drug in the donor's blood would be diluted by the recipient's blood and body fluids so that the recipient's blood level would be less than 10% of the donor's blood level of the drug. Patients under anesthesia would not be affected by 500 cc. of such blood. The only patients who might be adversely affected would be infants receiving exchange transfusions and patients allergic to the drug involved. These patients should not receive blood that contains these drugs.

ARTHRITIS AND VACCINE THERAPY

To the Editor:—*Are Coley's fluid and such bacterial vaccines as Cutter's "B. I. P." (Sherwood's formula) used in the therapy of arthritis?*

Charles R. Wylie, M.D., Los Angeles.

Answer.—During a long period in the first quarter of this century attempts were made to influence the course of rheumatoid arthritis with vaccines, either as protein shock therapy, active immunization therapy, or desensitization therapy. There is today, among well-trained rheumatologists, complete silence on the subject. Vaccines are of little or no value in the treatment of true rheumatoid arthritis. Coley's fluid has been used as a protein shock type of therapy (as was intravenous typhoid vaccine), but its use has never been seriously advocated.

ENURESIS

To the Editor:—*Is there justification for the use of meprobamate in the treatment of a patient with enuresis?*

Frank A. Andrews, M.D., Coldwater, Mich.

Answer.—There is no evidence that meprobamate is effective in the treatment of enuresis. The history of the treatment of enuresis abounds in various drugs and regimens which have been reported to be effective. It is likely that the most important ingredient of all has been the concurrent emotional care given the child and the family by the physician. If the child has at times been continent, the problem may be effectively managed by the general physician or pediatrician; but if the enuresis has been constant from infancy, psychiatric management is often necessary.

OMISSION OF LABORATORY TESTS

To the Editor:—*Should such difficult laboratory examinations as barium enema, pyelography, aortography, encephalography, and chest x-ray be done on elderly patients who are feeble and asthenic? The pain, discomfort, and excitement are often more deleterious to the patient than the benefits derived from the examinations.*

M.D., Kansas.

Answer.—Patients who have had recent myocardial infarction or who are enfeebled by age should be asked to endure procedures only when there is an anticipated operation for the correction of any lesion discovered. Search for primary tumors, when metastases are widespread and confirmed by cell study, is not to be done except for justified academic study.

IODINE SUPPLEMENTS

To the Editor:—*Is the dispensing of iodine tablets to children of school age necessary, in an area in which the natural iodine content of the soil and water is low, or is the use of iodized salt sufficient?*

C. M. Smith, M.D., Provo, Utah.

Answer.—Since iodine is an essential nutrient for persons of all ages, it appears preferable to provide it as a part of the ordinary diet rather than as a medicament for school children only. Accordingly, we would endorse the recommendation of the Utah State Medical Association and suggest that those living in the state use iodized salt routinely. It probably would be well also to make sure that the cows from whom milk for infant feeding is obtained are given iodized salt to lick.

MARIHUANA

To the Editor:—*The federal narcotics license entitles the holder to dispense marihuana. For what clinical conditions is this a therapeutic agent?*

James A. Brussel, M.D., New York.

Answer.—Marihuana, or cannabis indica, is no longer regarded as a valid therapeutic drug. It had been used as a fluid extract for its purported sedative or local analgesic effects. The growth, manufacture, sale, and dispensing of marihuana is controlled by the Marihuana Tax Act. The law provides the regulations under which the drug may be produced, transferred, or prescribed. Since cannabis has no medical use, the main purpose of the law is to provide a basis for legal prevention of illicit traffic in the drug.

AIR IN SUBMARINES

To the Editor:—*What system is used for maintenance of respirable gases in an atomic submarine?*

Lyman C. Blair, M.D., Houston, Texas.

Answer.—Adequate oxygenation of the air for an atomic submarine is provided by addition of the gas from stores of liquid oxygen, which makes possible storage of quantities adequate for long-duration submergence. Removal of carbon dioxide and other gaseous contaminants is accomplished by a "gas-scrubbing" process in which the submarine atmosphere is pumped through sea water and the dissolved gases are discarded. The method avoids the problems of chemical replacement or renovation that are inherent in older methods which use metallic alkali absorbents.

FILLING OF BONE CAVITIES

To the Editor:—*What is the use of plaster of paris in the treatment of bone cysts?*

Leon A. Frankel, M.D., Philadelphia.

Answer.—Plaster of paris has been used for many years in Europe to fill bony defects, such as those due to cysts or resections of bone for tuberculosis, osteomyelitis, tumor, and nonunion of fractures. This procedure is not used much in the United States. The paper by L. F. Peltier and others in *Annals of Surgery* (146:61-69 [July] 1957) outlines in detail the experimental and clinical use of plaster of paris.

WASHINGTON NEWS

Medicare Expanded . .
Food Chemical Programs . .
Taxes on Aged Persons . .
MD Radio Bands . .

MEDICARE BENEFITS RESTORED

The Defense Department formally announced the restoration of benefits that were chopped out of the Medicare program in an economy move more than a year ago. The new benefits will go into effect Jan. 1, 1960.

The defense agency said, however, that a permit system for dependents, inaugurated in October, 1958, will continue to be part of the Medicare program of providing treatment in civilian hospitals for qualified dependents of military personnel. Under the permit system dependents living with sponsors must use military medical facilities unless permits certify these are unavailable.

The reason for the liberalization is that Congress last summer voted the full $88,800,000 sought to run the Medicare program. Restored services include:

Treatment for patients with such illnesses as tonsilitis and hernia, which are not strictly of an emergency nature but for which good medical practice dictates prompt attention.

Care for acute emotional disorders for a period of 21 days or until other provision is made for more prolonged care.

Emergency outpatient care for acute injuries or accidents, such as simple fractures which do not require hospitalization.

The allowance of $75 for certain diagnostic tests, such as x-ray examination, has been restored in cases in which these tests eventually lead to hospitalization of the dependent. Similarly, the $50 allowance for certain posthospitalization procedures such as a blood transfusion for a leukemia patient before he is finally released as completely treated, has been restored.

These two allowances have been restored to allow flexibility for the complete care of a patient for whom hospitalization has been authorized, according to the department.

The Defense Department planned to issue shortly a revised directive on Medicare, which the services will implement with their own regulation. The office for dependents' medical care will also send revised instructions to its contractors concerning payments to physicians and participating hospitals.

FOOD CHEMICAL CONTROVERSY

The problem of chemicals in food, highlighted by the recent contaminated cranberry incident, has been receiving increasing federal attention.

Two relatively new laws have given the Food and Drug Administration broader powers to regulate such chemicals, and there are indications that the cranberry episode may have been the first of a series of controversies.

FDA has set a March 6, 1960, deadline for food processors and chemical manufacturers to submit information to the government showing that the chemical additives in their products are safe for human consumption. Chemical additives are used to color, preserve, and enrich food and have been used extensively since World War II.

Some officials said that it appears that many manufacturers would not be able to meet the deadline and that some foods may have to be withdrawn from the market as a result.

The so-called food additives bill approved by Congress last year gave FDA for the first time the power to require that manufacturers prove the safety of the chemical additives they use. Previously, it was the responsibility of the government to prove that the additives were dangerous.

Another recent law gave FDA the authority to regulate pesticides used on fruits and vegetables. One such pesticide, aminotriazole, was found to have contaminated some cranberry crops.

The reason for the drastic federal action in seizing cranberry shipments was that an amendment to the chemical additives law specified that any chemical that causes cancer in animals cannot be present in food, however small the amount. FDA discovered last May that aminotriazole causes cancer in rats if fed in sufficient quantity.

FDA recently announced that 182 chemicals have been found safe for use in food and that manufacturers who use these chemicals do not have to furnish further proof of their safety. However, tolerance levels were set on some of these chemicals.

At the same time, the agency said further consideration is needed for six materials: four food coloring materials, carbon black, charcoal, titanium dioxide, and ultramarine blue; oleic acid; and linolic acid. FDA emphasized that these substances are not necessarily unsafe but that further review is needed.

The list of 182 safe food chemicals, as judged by scientists across the country in reply to a questionnaire, included 28 preservatives, 37 buffers and neutralizing agents, 9 emulsifiers, 5 non-nutritive sweeteners, 35 nutrients, 29 sequestrants, and 30 multipurpose products.

In another field of regulation, an FDA order has stirred the lipstick industry to charge that it might be seriously damaged. The order proposes to ban 17 coal-tar dyes used in coloring shades of lipstick. FDA took the action because of a court decision that, under the law, FDA, in ruling on the safety of coal-tar colors, can only decide that they are harmful or not harmful. As interpreted by FDA this has meant that no matter how minute the quantity of a coal-tar color present in a product, the color must be banned if it can cause any harm in any quantity when given to test animals.

As a result of the court decision, the administration has asked Congress for the authority to set tolerance levels—maximum amounts permitted—for coal-tar colors.

Meanwhile, Sen. Vance Hartke (D., Ind.), chairman of a Senate commerce subcommittee, predicted that the group would act early next year on a House-passed measure requiring the labeling of household substances such as cleansers that are highly toxic or inflammable. The American Medical Association has urged favorable congressional action on the measure to help prevent accidental poisonings, especially among children.

SPECIAL TAX TREATMENT FOR AGED HIT BY FORAND BILL BACKERS

Two leading supporters of the controversial Forand bill told the House Ways and Means Committee that the government should not help the elderly through special income tax treatment.

Wilbur M. Cohen, professor of public welfare administration at the University of Michigan and a frequent consultant to congressional committees, said the solution to the problem of the elderly is through extension of the Social Security program to partially finance health care for the aged and through purchase of hospitalization insurance for aged persons who are not under the social security system.

Renewing his backing of the principle of the Forand bill, which is opposed by the American Medical Association, the administration, the insurance industry, and numerous allied groups, Cohen said that if the Social Security health bill is approved, present tax concessions for the elderly actually could be eliminated or modified.

Eviline M. Burns, professor of social work at Columbia University, also said "the only effective way" of meeting the medical needs of the aged is by broadening the social security program through higher taxes on employers and employees alike.

The Ways and Means Committee, which took no action on the Forand proposal last session, conducted hearings on over-all income tax revisions during the recess. A part of these hearings were devoted to income tax treatment of the aged.

Committee Chairman Wilbur Mills (D., Ark.) asked Cohen if a retired couple past 65 years of age, with a $5,000 annual income, has less ability to pay taxes than a young married couple with the same income. Cohen said the aged couple is much better able to pay the taxes than the younger couple, since they have already paid for their home and other durable goods. He testified that he saw no reason for deductions for medical care for the aged when young people were not getting as many deductions. Miss Burns agreed.

Cohen flatly declared that "The federal budget in the future will be carrying a sizable and increasing financial burden for medical care costs for aged persons."

"Voluntary health insurance does not adequately cover the medical needs of aged persons . . . and is not likely to cover all or most low-income aged persons in the foreseeable future," said Cohen.

The administration, the A. M. A., and other organizations have pointed out that rapid strides are being made in the field of voluntary insurance and that such progress would be canceled if a federal program were instituted. In addition, they have noted the high rate of social security taxes that workers and employers would have to pay to bear the burden of the larger social security role envisaged in the Forand proposal.

GOVERNMENT OPENS PROCEEDINGS ON PHYSICIANS RADIO BANDS

The Federal Communications Commission agreed to hold formal proceedings on the American Medical Association's request that certain radio frequencies be set aside for emergency use by physicians.

The agency called for comments from all interested parties on the proposal and set a Feb. 1, 1960, deadline for the submission of comments for and against the proposal.

In the order, the FCC asked for suggestions on a proposed set of rules reserving 13 frequencies on the 150-megacycle band and 4 on the 40-megacycle band. The A. M. A. had asked for 10 and 2 frequencies, respectively, and the American Hospital Association had sought 3 and 2 on the respective bands. There are many similarities between the A. M. A. and the AHA requests.

A major purpose of the frequency reservation would be to enable physicians to keep in close contact while at home, at the office, and in their automobiles, with a reserved radio frequency that could alert them to emergency calls usually relayed through a central medical bureau.

After the comments are filed, the FCC will decide what further action to take on the petitions.

MISCELLANY

The Public Health Service dispatched telegrams to all state health officers urging them to warn owners of small travel trailers which might be equipped with a small bottled gas heater that apparently caused eight deaths this year. The Thurm Heater, manufactured by the Thurm Engineering Co., Elkhart, Ind., "has been shown to be of faulty design and is capable of building up a lethal concentration of carbon monoxide gas within a trailer in a very short time," according to PHS.

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Doses of 5 mg. at intervals of six to eight hours provide effective relief all day. Suggestion: first tablet to be taken upon awakening.

For patients unable to retain oral medication when first seen, Mornidine may be administered intramuscularly in doses of 5 mg. (1 cc.).

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

December

American Academy of Dermatology and Syphilology, Palmer House, Chicago, Dec. 5-10. Dr. Robert R. Kierland, First National Bank Bldg., Rochester, Minn., Secretary-Treasurer.

American Association for the Advancement of Science, Morrison Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. of Virginia, Richmond, Va., Director of Public Information.

American Psychoanalytic Association, Biltmore Hotel, New York City, Dec. 4-6. Dr. David Beres, 151 Central Park West, New York 23, Secretary.

American Rheumatism Association, Henry Ford Hospital, Detroit, Michigan, Dec. 11. Gerard W. Speyer, 10 Columbus Circle, New York 19, Executive Secretary.

Association for Research in Nervous and Mental Disease, Inc., Hotel Roosevelt, New York City, Dec. 11-12. Dr. Rollo J. Masselink, 700 W. 168th St., New York 32, Secretary-Treasurer.

New York Heart Association, Symposium on Salt and Water Metabolism, Biltmore Hotel, New York City, Dec. 11-12. Dr. Alfred P. Fishman, N. Y. Heart Association, 10 Columbus Circle, New York City, Chairman.

New York State Society of Anesthesiologists, Inc., Postgraduate Assembly in Anesthesiology, Hotel New Yorker, New York City, Dec. 9-12. Dr. Edwin J. DePolo, 131 W. 11th St., New York 11, Secretary.

Southern Surgical Association, The Homestead, Hot Springs, Va., Dec. 8-10. Dr. John D. Martin Jr., Emory Univ., Box 459, Atlanta 22, Ga., Secretary.

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Mid-Winter Clinical Convention for Ophthalmologists and Otolaryngologists (29th), Research Study Club, Ambassador Hotel, Los Angeles, Jan. 17-22. Dr. Norman Jesberg, 500 S. Lucas Ave., Los Angeles 17, Secretary-Treasurer.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz., Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel,
Beach, Fla., Feb. 1-5. For information write: Clinical Congr
Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House,
cago, Feb. 7-9. For information write: Council on Medical Edu
and Hospitals, American Medical Association, 535 N. Dearbor
Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Me
Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memp
Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, D
Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschge
Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern Calif
Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd
Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr
Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), Univers
Texas, Houston, Feb. 25-27. For information write: University of
M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas

March

American Broncho-Esophagological Association, Deauville
Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locu
Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Ch
Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secr
Treasurer.

American Academy of General Practice, Philadelphia, Mar.
Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12,
Executive Director.

American Association for the History of Medicine, Inc., Charl
S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Instit
Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broad
Colorado Springs, Colo., Mar. 21-23. For information write: Dr.
Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Po
Hotel, Portland, Ore., Mar. 28-30. For information write: Dr.
Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel,
Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Un
Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Ma
Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Trea

American Laryngological Association, Deauville Hotel, Miami
Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of
nology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Soc
Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. St
Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach,
Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minne
14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Dea
Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Ba
Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel,
real, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt,
Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto
Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory
versity, Atlanta 22, Ga., Secretary.

Missouri State Medical Association, Sheraton-Jefferson Hotel
Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Lo
Executive Secretary.

National Health Council, National Health Forum, Miami,
Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, E
tive Director.

National Multiple Sclerosis Society, New York City, Mar. 8.
Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Ma
Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimo
Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel,
Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave.,
Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans,
21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Exec
Secretary.

Southwestern Surgical Congress, Riviera Hotel, Las Vegas, Nev.,
28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma
Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral Sem
Hotel, Mobile, Apr. 21-23. Mr. W. A. Dozier Jr., 19 S. Jackson
Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla.,
25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Exec
Secretary.

American Association of Anatomists, Statler-Hilton, New York
Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Medi
Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Immunologists, Chicago, Apr. 11-15.
Calderon Howe, Columbia Univ. College of Physicians and Surg
New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists,
Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. Holman,
of Pathology, L. S. U. School of Medicine, New Orleans, La., Secre

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TREATMENT OF IDIOPATHIC THROMBOCYTOPENIC PURPURA

Alan F. Carpenter, M.D., Maxwell M. Wintrobe, M.D., Ph.D., Ellis A. Fuller, M.D., Arthur Haut, M.D.
and
George E. Cartwright, M.D., Salt Lake City

IDIOPATHIC thrombocytopenic purpura (ITP) is a disorder of unknown etiology and pathogenesis. That some cases appear to be self-limited, whereas others run a more chronic course necessitating vigorous therapy, may indicate that the disease results from one of several causes. Prior to the availability of the adrenocortical steroids for the treatment of ITP, major therapeutic reliance was placed on splenectomy, a procedure frequently followed by a complete remission.[1] With increasing experience in the use of prednisone and other adrenocortical steroids the therapeutic superiority of splenectomy in ITP has been challenged.[2] Certain possible disadvantages of splenectomy have been cited. These include (1) "the strong possibility of dissemination of the lupus [erythematosus] process following splenectomy"[3]; (2) the "high relapse rate following splenectomy"[4]; and (3) "the hazards of severe infections in splenectomized infants and children . . . in the immediate and remote postoperative period."[5]

The present report is concerned with 85 consecutive cases of ITP seen in the hematology division of the department of medicine of the Salt Lake County General Hospital between July, 1945, and April, 1959. The major purpose of the study was to review and analyze our experiences in the treatment of this

The course of idiopathic thrombocytopenic purpura (ITP) was studied in four groups of patients. In the first group of 24 patients the therapy did not include either steroids or splenectomy, but 10 had complete remissions within a year after the ITP was recognized. All 10 were less than 10 years of age and each had had an infection within a month before the onset of the ITP. The second group consisted of 16 patients who received steroids without splenectomy; the third consisted of 26 who did not receive steroids but underwent splenectomy. The fourth group, consisting of 19 patients, were treated both with steroids and by splenectomy. Complete remissions were obtained in 25 (81%) of the splenectomized patients and only 11 (38%) of the patients treated with steroids. Splenectomy gave better results than did steroids in the dosages used, but there were three serious postoperative infections, and in one case lupus erythematosus appeared 12 months after the splenectomy.

From the Department of Medicine, College of Medicine, University of Utah.

disorder. Concurrently our data have been evaluated with respect to the cautions and deterrents to splenectomy cited above.

Materials and Methods

Patients with thrombocytopenic purpura were excluded from this series if adequate historical or laboratory documentation was lacking or if there was any doubt concerning the final diagnosis. Cases of thrombocytopenic purpura which developed after a viral or other infection have been included in the analysis. No cases of thrombocytopenic purpura have been included if the disease was thought to be an effect of an ingested drug or toxin or to be secondary to another disease process; e. g., sarcoid, disseminated lupus erythematosus, leukemia, or marrow invasion with neoplastic cells. Other patients have been excluded if histopathological review of splenectomy material revealed an abnormality not usually encountered in ITP; e. g., one with infiltration of the spleen by non-lipid-containing foamy macrophages and one with myeloid metaplasia. Because isolated thrombocytopenic purpura may be the initial manifestation of disseminated lupus erythematosus,[3] all patients with cases initially thought to represent ITP were reviewed for the appearance of manifestations of disseminated lupus erythematosus after splenectomy.

TABLE 1.—*Analysis of Case Data in Ten Patients with Self-Limited and Fourteen with Unremitting Cases of ITP Given No Treatment*

	No. of Patients	Prior Infection	Age, Yr.			Duration of ITP at Last Observation or at Onset of Remission, Mo.		
			<10	10-25	>25	<1	1-12	>12
Spontaneous remissions	10	10	10	0	0	6	4*	0
Unremitting ITP, alive	12	1	2	6	4	2	9	8
Unremitting ITP, dead	2	0	0	1	1†	1	1†	0

* Duration of ITP was 2 mo., 7 mo., and 12 mo., respectively, in three and unknown in the fourth.

† Atypical ITP with malaise, headaches, and anemia in patient aged 49 on whom no autopsy was performed.

Analysis of Case Material.—In the following analysis, the term "complete remission" indicates a permanent supervention of complete clinical and hematological normalcy. The term "partial remission" indicates the development of a clinical state exhibiting significantly less severe symptomatic or laboratory abnormalities than were present previously.

Division of Case Material into Groups for Subsequent Analysis: For the purpose of analysis of the final outcome of the disease with or without therapy, the patients were allocated to one of four mutually exclusive groups. Group 1 consisted of patients neither receiving adrenocortical steroids nor undergoing splenectomy; group 2 consisted of patients undergoing steroid therapy without splenectomy; group 3 consisted of patients undergoing splenectomy without steroid therapy at any time; and group 4 consisted of patients treated both with steroids and by splenectomy.

Group 1.—Included in the group of those receiving therapy neither with steroids nor by splenectomy are 24 patients (table 1). Of these, 10 underwent complete remission one week to 12 months after ITP was first recognized. These 10 patients who had a complete spontaneous remission were remarkable in that they were all less than 10 years of age and also in that in all a history could be obtained of a preceding infection within one month of the onset of their disease.

Of the remaining 14 patients in group 1 (table 1), namely, those who at the time of their last follow-up visit still showed evidence of their disease, only one gave a history of infection shortly before the onset of his purpura and 12 were more than 10 years of age. Eight were known to have had ITP for longer than 12 months.

The 2 deaths in this entire series of 85 cases were in this group, and both were due to spontaneous intracerebral hemorrhage occurring after two weeks and six weeks of ITP respectively (table 1).

Group 2.—Included in the group of those receiving steroid therapy without splenectomy are 16 patients. Of these, 11 received one of the newer synthetic adrenocortical steroids (table 2). Of these 16, 10 had complete remission of the disease (table 3). Of these 10, 8 were less than 10 years of age. The total duration of the disease at the time of remission was four months or less in all 10.

Further analysis of the cases of these 10 patients reveals that 2 entered remission while steroid therapy was being discontinued because of its failure to produce an effect after therapeutic courses of 3 and 14 weeks respectively. In another case steroids were given for only two days, being prescribed because of the appearance of localized neurological signs during a period when the patient's platelet count was already rising. The remaining seven patients who had complete remissions received steroids for a period ranging from two to six weeks. The youth and the short course of the illness in all of those who had remissions are compatible with the patient age and disease duration of those who had spontaneous remissions. Also, like many of those with cases of self-limited ITP, 6 of the 10 patients who developed a complete remission associated with steroid therapy had had a manifest infection just prior to the onset of their disease.

TABLE 2.—*Correlation of Disease with Therapy in Sixteen Patients Treated with Steroids Only*

Steroid Preparation	No. of Patients	Daily Dose, Mg.	Duration of Therapy	Remissions, No.	Persistent ITP, No.
Prednisone	8	15-40	2 days-66 mo.	5	3
Prednisolone	2	40	3-6 wk.	1	1
Methylprednisone	1	4	9 mo.	0	1
Cortisone	5	50-200	2-12 wk.	4	1

In three of the six who did not have remission of the disease with steroid therapy, the course of treatment was limited to two weeks. These three had had their disease for less than two months at the time of the last follow-up examination, were less than 10 years of age, and had had prior infection. Thus they resembled the patients in whom a spontaneous remission might develop. The remaining three who failed to have remissions with steroid therapy have been observed in continued relapse for more than one year after treatment of two weeks' to 66 months' duration.

Group 3.—The group of those treated by splenectomy without steroids includes 26 patients (table 4). Of these, 17 have had a lasting, complete remission from their disease after splenectomy and their progress has been followed for 12 months or more postoperatively. There are three patients with postsplenectomy follow-up of more than 12 months who have had no favorable response to splenectomy, who are classified as having "splenectomy failures."

The response to splenectomy in the remaining six patients has not been tabulated either because the progress of the patients was followed for less than one year after splenectomy or because the patients were referred here because of the failure of splenectomy to induce a remission. Three of these showed an early favorable response to splenectomy but were last seen within 12 months of operation. A fourth has had a symptomatic remission from his disease, with follow-up of more than 12 months after operation, but was referred to us because of intermittent postoperative thrombocytopenia, with platelet counts varying between 90,000 and 250,000 per cubic millimeter. The fifth patient has had a partial response to splenectomy but was last seen five months after operation. The sixth patient in this unclassified group was referred to us because of the failure of splenectomy to effect a cure. Because of the referral bias the fourth and sixth cases have not been included in the statistics relating to operative success or failure. There were no deaths attributable to splenectomy.

TABLE 3.—*Correlation of Results of Therapy and Age in Sixteen Patients Receiving Therapy with Adrenocortical Steroids Only*

	No. of Patients	Duration of ITP at Time of Last Follow-up, Mo.			Age at Onset of ITP, Yr.			Duration of Steroid Therapy, Wk.		
		<2	2-12	>12	<10	10-25	>25	<2	2-6	>6
No. of remissions	10	9	1	0	8	2*	0	1	8	1
No. of unremitting cases	6	3	0	3	4	0	2	4	0	2

* 18 and 23 years of age respectively.

Eliminating those patients with a referral bias toward splenectomy failure, and eliminating those patients with postsplenectomy follow-up of less than one year, the statistics outlined in table 5 are derived.

When the group of patients with successful splenectomies (table 4) is analyzed in terms of age, duration of disease, and presence or absence of antecedent infection, it is evident that only three patients were over 25 years of age; the total duration of the disease at the time of splenectomy was less than one year in 10; three had had their disease for more than 143 months; and the longest duration of the disease in a patient responding favorably to splenectomy was 247 months. From the analysis of self-limited ITP it has been seen that patients who are less than 11 years of age and have had purpura for less than 12 months may enter complete remission spontaneously. Three of the patients with successful results of splenectomy may, therefore, have been expected to recover spontaneously, in view of their young age and the short duration of their disease. None of the patients with "splenectomy failures" might have been expected to recover spontaneously by these criteria. As to antecedent infection, three of the patients with "splenectomy successes" gave a history of infection immediately prior to the onset of their disease, but none of those with "splenectomy failures" gave a history of antecedent infection.

TABLE 4.—*Correlation of Results with Age of Patient and Duration of Disease in Twenty-six Patients Treated by Splenectomy Only*

Result	No. of Patients	Duration of Postsplenectomy Follow-up, Yr.				Age at Splenectomy, Yr.			Duration of ITP Before Splenectomy, Yr.		
		<1	1-3	3-8	>8	<10	10-25	>25	<1	1-4	>4
Complete remission	17	0	6	5	6	3	11	3	10	4	3
Continued ITP	3	0	1	2	0	1	0	2	0	1	2†
Referral bias or brief follow-up	6	4*	0	1	1	1	3	2	3	1	2‡

* 7 mo., 5 mo., 1 wk., 1 wk.
† 460 mo., 80 mo.
‡ 143 mo., 52 mo.

Group 4.—It is difficult to analyze the results of therapy in the group of 19 patients treated both with steroids and by splenectomy. Taking first the steroid therapy, presplenectomy therapy was given to 16 patients. In only one was there an apparent complete response to this treatment. However, splenectomy was performed immediately after this optimal steroid response, at the insistence of the child's parents, and follow-up data are therefore incomplete with reference to the permanence of the steroid effect. This patient will be considered arbitrarily as an illustration of "steroid success," whose progress was inadequately followed; however, this was a 4½-year-old girl who had had idiopathic thrombocytopenic purpura for only one month and might well have had a spontaneous remission.

In five cases steroid therapy was given after splenectomy. Two of these patients had received preoperative therapy as well. In three this was of no benefit; in the fourth case there was transient symptomatic benefit only; and in the fifth the disease eventually underwent complete remission, and it cannot be stated whether splenectomy or steroid therapy should be credited with the production of the remission. In view of the unusual nature of this disorder. Concurrently our data have been evaluated with respect to the cautions and deterrents to splenectomy cited above.

Materials and Methods

Patients with thrombocytopenic purpura were excluded from this series if adequate historical or laboratory documentation was lacking or if there was any doubt concerning the final diagnosis. Cases of thrombocytopenic purpura which developed after a viral or other infection have been included in the analysis. No cases of thrombocytopenic purpura have been included if the disease was thought to be an effect of an ingested drug or toxin or to be secondary to another disease process; e. g., sarcoid, disseminated lupus erythematosus, leukemia, or marrow invasion with neoplastic cells. Other patients have been excluded if histopathological review of splenectomy material revealed an abnormality not usually encountered in ITP; e. g., one with infiltration of the spleen by non-lipid-containing foamy macrophages and one with myeloid metaplasia. Because isolated thrombocytopenic purpura may be the initial manifestation of disseminated lupus erythematosus,[3] all patients with cases initially thought to represent ITP were reviewed for the appearance of manifestations of disseminated lupus erythematosus after splenectomy.

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Complete remission	17	0	6	5	6	3	11	3	10	4	3
Continued ITP	3	0	1	2	0	1	0	2	0	1	2†
Referral bias or brief follow-up	6	4*	0	1	1	1	3	2	3	1	2‡

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‡ 143 mo., 52 mo.

Group 4.—It is difficult to analyze the results of therapy in the group of 19 patients treated both with steroids and by splenectomy. Taking first the steroid therapy, presplenectomy therapy was given to 16 patients. In only one was there an apparent complete response to this treatment. However, splenectomy was performed immediately after this optimal steroid response, at the insistence of the child's parents, and follow-up data are therefore incomplete with reference to the permanence of the steroid effect. This patient will be considered arbitrarily as an illustration of "steroid success," whose progress was inadequately followed; however, this was a 4½-year-old girl who had had idiopathic thrombocytopenic purpura for only one month and might well have had a spontaneous remission.

In five cases steroid therapy was given after splenectomy. Two of these patients had received preoperative therapy as well. In three this was of no benefit; in the fourth case there was transient symptomatic benefit only; and in the fifth the disease eventually underwent complete remission, and it cannot be stated whether splenectomy or steroid therapy should be credited with the production of the remission. In view of the unusual nature of this delayed response to splenectomy alone, this patient will be considered to represent a case of steroid-induced remission.

Thus, in this group of 19 patients treated both with steroids and by splenectomy, 2 may have responded to the steroid medication rather than to the splenectomy. Only one of these two has maintained her remission status subsequent to steroid withdrawal, the criterion for inclusion as an example of successful steroid therapy.

TABLE 5.—*Results of Splenectomy in Twenty-six Patients Not Treated with Adrenocortical Steroids*

	No.	%
Total no. of patients undergoing splenectomy	26	..
Patients followed less than 12 mo. postoperatively	4	..
Patients with referral bias	2	..
Net total splenectomies*	20	100
Complete remissions	17	85
Partial remissions	0	0
Failures	3	15

* See text for explanation of those deleted from analysis.

Of the remaining 17 (table 6), the progress of 4 has been followed less than 12 months since splenectomy and will not be included in the statistical evaluation of the effect of surgical therapy. The derivation of this time interval for postoperative evaluation is based on the observation of one patient who entered remission six months after splenectomy; consequently postoperative follow-up of less than one year may be inadequate for ultimate evaluation. It may be added that the inclusion of the patients whose course is known for less than one year does not alter the cumulative statistics concerning the outcome after splenectomy. Two more patients, both with evidence of ITP continuing after splenectomy, were referred to us because of this operative failure. Because of this referral bias they will be excluded from the tabulation of the statistics with regard to splenectomy.

Of the original 19 patients in group 4 there remain 11 for whom adequate follow-up data are available for the assessment of the effects of splenectomy. Eight have had complete postsplenectomy remissions; two are classified as having partial postsplenectomy remissions; and one has a "splenectomy failure." Of the 19 patients in group 4, 5 were referred to us partly because of the failure of steroid medication to induce a remission. These five were excluded from the tabulation of the results of steroid therapy because of the bias introduced.

Final Results.—The analysis of the results of therapy in the 19 patients in group 4 is presented in table 7. When these figures are combined with those derived from the analyses of groups 2 and 3, the statistics shown in table 8 are produced.

Comment

The figures as tabulated are impressive evidence for the superiority of splenectomy in the treatment of unremitting idiopathic thrombocytopenic purpura, as compared with steroid therapy. Our use of steroid therapy has not been as vigorous as that advocated by others.[6] However, the success of splenectomy in our patients, taken together with the known complications of prolonged treatment with large doses of adrenocortical steroids, has caused us to recommend splenectomy for all patients with persistent cases of ITP.

Of our 27 patients who underwent splenectomy and were in complete remission 12 months after operation, 2 (7.4%) subsequently relapsed and therefore have been classified in table 8 as having responded partially to splenectomy. These relapses occurred 24 and 28 months after splenectomy respectively. Of the above 27 patients with successful splenectomy, the progress of 17 has been followed for three years or more. If the 2 patients with late relapses are charged against these 17 with an equivalent duration of follow-up, the relapse rate becomes 11.8%. Thus, in our experience postsplenectomy relapse is an occasional occurrence but is not so frequent that it acts as a deterrent to the recommendation of splenectomy for treatment of patients with ITP.

We have observed only one patient (not included in the series of 85 with cases of ITP) who developed disseminated lupus erythematosus (DLE) after undergoing splenectomy. The characteristic lupus syndrome did not appear until 12 months after splenectomy, which was performed after three years of thrombocytopenic purpura. That this 13-year-old girl probably had DLE prior to splenectomy was suspected because of the presence of prolonged moderate leukopenia and a weakly positive result of the serologic test for syphilis during the period of preoperative observation. Therefore, at least insofar as patients without evidence of lupus prior to splenectomy are concerned, we have not uncovered evidence that there is a "strong possibility of dissemination of the lupus process following splenectomy"[3] for ITP.

TABLE 6.—*Correlation of Results, Age of Patient, and Duration of Disease in Seventeen Patients Treated Both with Steroids and by Splenectomy*

Result	Patients, No.	Duration of Postsplenectomy Follow-up, Yr.			Age at Splenectomy, Yr.			Duration of ITP Before Splenectomy, Yr.		
		<1	1-3	>3	<10	10-25	>25	<1	1-4	>4
Complete remissions	8	0	4	4	4	1	3	6	2	0
Continued ITP	3	0	1	2	2	0	1	0	3	0
Referral bias or brief follow-up	6	4	1	1	2	4	0	2	2	2

Of the 45 patients who underwent splenectomy 3 had postoperative infections that were severe enough to be remembered by the patient or his family on follow-up examination. These were (1) primary atypical pneumonia six years after operation, with recovery, in a 43-year-old man; (2) "mild" pneumonitis five years after operation, with recovery, in an 18-year-old girl; and (3) pneumococcic septicemia leading to death in a 41-year-old woman eight years after splenectomy. There were no serious infections observed after splenectomy in the 23 patients who were less than 15 years of age at the time of operation. Thus we have no data which might suggest that splenectomy should be avoided because of the "hazard of severe infections . . . in the immediate and remote post-operative period."[5]

In 25 patients who did not have complete remission either spontaneously or during steroid administration, 13 were benefited symptomatically by steroid therapy. Confirmation of this improved status was afforded by the development of a negative result of the tourniquet test, by a shortening of the prolonged bleeding time, or by a rise to subnormal levels in the circulating platelets. This observation has led us to prescribe steroids occasionally for some patients with symptomatic ITP during the period of preoperative observation, if the patient is not hospitalized.

One of the patients in group 2 who was categorized as having developed a complete remission while receiving steroid therapy was 23 years of age and entered remission during the discontinuation of apparently ineffective steroid therapy one month after the onset of ITP. In a second patient in group 2 the platelet count was already rising before steroids were prescribed for a two-day period. This 18-year-old boy showed no evidence of ITP thereafter. A third patient in group 2 also had remission during the period of withdrawal of apparently ineffective steroid therapy. Although these three patients have been classified as having had complete remission as a result of steroid therapy, it might be more reasonable to allocate them to the group of those who had spontaneous remissions. Regrouping these 3 patients in this way, it is seen that 2 (15%) of the 13 patients with "spontaneous" remissions were between the ages of 10 and 25 years. It seems likely, therefore, that an occasional spontaneous remission will be seen even in patients up to 23 years of age, especially when there is a history of infection prior to the development of the disease. Furthermore, since 2 of the 10 spontaneous remissions in group 1 occurred in patients who had had ITP for 7 and 12 months, respectively, we now believe that it is worth while to observe young patients expectantly for the development of a remission for a 12-month period.

TABLE 7.—*Analysis of Results of Therapy in Nineteen Patients Treated Both with Adrenocortical Steroids and by Splenectomy*

Total no. of patients given steroids	19
Patients treated with steroids but excluded from analysis	6
Patients followed up too briefly for categorization of response to therapy	1
Patients with referral bias	5
Net patients treated with steroids and analyzed	13
Complete remissions	1
Failures and incomplete responses	12
Total no. of patients undergoing splenectomy	19
Patients excluded from analysis	8
Responses attributed to steroids	2
Patients followed up too briefly for categorization of response to therapy	4
Patients with referral bias	2
Net patients with splenectomies analyzed	11
Complete remissions	8
Partial remissions	2
Failures	1

TABLE 8.—*Analysis of Results of Therapy in Sixty Patients Treated Either with Adrenocortical Steroids or by Splenectomy, or Both (Groups 2, 3, and 4)*

	No.	%
Total no. of patients treated by splenectomy	31	100
Complete remissions	25	81
Partial remissions	2	6
Total benefited	27	87
Failures	4	13
Total no. of patients treated with steroids*	29	100
Complete remissions	11	38
Failures and transient improvement	18	62

* This figure is derived by giving benefit of doubt to steroid causation of remission, in each case in which this might have been a possibility

No spontaneous remissions were observed after ITP had been present for more than 12 months. Only one of the 11 possibly steroid-induced remissions occurred after more than one year of ITP. Of the 25 complete postsplenectomy remissions 16 (64%) occurred within 12 months of the onset of the disease, and there were no "splenectomy failures" among those patients operated on during the first 12 months of ITP. In contrast, only 7 (64%) of the 11 splenectomies performed more than 24 months after the onset of ITP were completely successful. From this it might be concluded that the success of any therapy will be greatest if it is administered within the first 12 months of the disease and that the only reasonable chance for the production of a complete remission after that time is by splenectomy.

Of our 85 patients with ITP 18 have had bleeding episodes sufficiently serious to require replacement transfusion. None of these developed clinical shock. Three more patients bled intracranially and two of these died (see group 1). The third patient developed a nonfatal intracerebral hemorrhage after trauma after six weeks of ITP. She was receiving treatment with cortisone at the time but the trauma may well have been sufficient to cause a similar hemorrhage in an otherwise healthy person. These data indicate that fatal hemorrhage is unusual in a patient with ITP of more than two months' duration. This should comfort the physician who hesitates to use adrenocortical steroid therapy for long periods of time in patients with unremitting ITP.

Summary and Conclusions

The progress of patients at least up to 11 years of age and perhaps up to 23 years of age, especially if there is a history of antecedent infection, should be followed for 7 to 12 months before abandoning the expectation of complete spontaneous remission from idiopathic thrombocytopenic purpura.

Steroid therapy alone in conventional doses has been associated with the development of complete remission in 38% of our cases, at best. A complete remission from idiopathic thrombocytopenic purpura followed splenectomy in 81% of our cases. Of the 11 patients categorized as having idiopathic thrombocytopenic purpura of two years' duration or longer at the time of splenectomy, 7 (64%) sustained a complete postoperative remission. There were no operative failures among the 16 patients with idiopathic thrombocytopenic purpura of less than 12 months' duration at time of splenectomy.

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TREATMENT OF BLEEDING ESOPHAGEAL VARICES

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When massive upper gastrointestinal bleeding occurs, esophageal varices must be considered as a possible cause. The Sengstaken tube, equipped with a balloon that can be inflated after it has reached the stomach, also permits aspiration of gastric contents. If used as here suggested it will generally stop hemorrhage due to esophageal varices or give diagnostic clues when the hemorrhage is from other sources. While it is in place the patient requires constant nursing care, and such tamponage if continued longer than 48 hours increases the risk of subsequent operation. The timing of the definitive surgery, location of the incision, and type of operation are decided by the patient's history, general condition, and laboratory tests. For patients who have bled repeatedly from proved esophageal varices, who are not jaundiced, and who show no signs of ammonia intoxication, the recommended operation is portacaval end-to-side anastomosis.

Portal hypertension is a complication of cirrhosis existing in a permanent form exclusively in human beings, as it cannot be reproduced, except in the most transient fashion, in laboratory animals, even by ligating the portal vein. If the animal survives the procedure, its portal pressure returns to normal in 10 days to three weeks. This affords us a clue as to the mechanism of portal hypertension, esophageal bleeding, and ascites. The experimental animal resists the development of these conditions because of the extensive system of retroperitoneal collateral veins which it possesses.[1] Some human beings are blessed with an extensive ramification of the veins of Retzius in the retroperitoneal tissues, and in these persons cirrhosis is not apt to be attended by the aforementioned complications (fig. 1).

Etiology of Esophageal Hemorrhage

The question that arises is: What is the precise mechanism of esophageal bleeding? This remains to be determined, as there is no experimental material available to prove the point. Portal hypertension is a variable thing, and it is conceivable that a simple increment in the already elevated portal pressure level, produced by sneezing, coughing, or

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From the Department of Surgery, Kaiser Foundation Hospital.

straining, may be sufficient to cause the distended, tortuous, thin-walled veins to rupture at their weakest point. On the other hand, many authorities believe that some specific form of trauma, such as that caused by a rough piece of toast or a bone grazing the esophageal mucosa, or the chemical erosion of alcohol, may be sufficient to cause hemorrhage. Another theory is that peptic esophagitis (extremely common in portal hypertension because of the distention of the cardioesophageal junction produced by the distended veins) with associated acid peptic regurgitation erodes the esophageal mucosa and the vein wall, causing rupture and hemorrhage.

I do not know the answer to this but have seen several patients with esophageal hemorrhage after gastrectomy with known gastric anacidity. Excessive degrees of portal hypertension, supplemented by any factor which may tend to raise the portal pressure transiently higher than its resting maximum, may cause a vein wall blowout, just as varicose veins of the lower extremity may blow out spontaneously. Anyone who has ever seen massive gastrointestinal bleeding from a ruptured esophageal varix will testify that it is an alarming and dramatic sight. The only patients who tend to exsanguinate more quickly are those in whom either a malignant tumor or gastric ulcer has eroded through the left gastric artery. When such a patient enters the emergency room of the hospital he presents a serious and difficult problem.

The most common cause of massive upper gastrointestinal bleeding is, of course, peptic ulcer. The second in order of frequency is bleeding esophageal varices and, taking the average throughout the nation, about one patient out of three who enters the hospital with a massive gastrointestinal hemorrhage is bleeding from varices. Most of the time the patient will be unknown to the emergency room physician or, for that matter, to anyone on duty at that moment. He may well be in deep shock or indeed in coma so that it is impossible to obtain a reliable history. The mere fact that he may arrive reeking of alcohol and with all the obvious clinical stigmata of cirrhosis, even with obvious ascites, may not clinch the diagnosis of bleeding varices, as it is well known that patients with cirrhosis have a much higher incidence of gastritis and peptic ulcer than the average population.

Emergency Diagnosis

Fortunately we can combine diagnosis and treatment almost immediately, if a Sengstaken tube (or one of the variations thereof) is kept on hand. Such a tube should be standard equipment in every hospital emergency room throughout the world. The tube is introduced through the nose, passed rapidly into the stomach, the gastric contents aspirated, and the gastric balloon inflated with 150 cc. of air. Strong traction is applied on the tube, and the traction is retained by means of one of several devices. As an emergency measure, it can be secured temporarily to the face with tape. The esophageal balloon is inflated to a pressure of 35 to 45 mm. Hg. This will require 50 to 75 cc. of air. The esophageal balloon tube is connected to a mercury manometer (with a three-way stop-cock introduced into the system to permit addition of air into the esophageal balloon to maintain pressure) so that variations in pressure are recorded constantly. Pressure will vary with motion of the diaphragm over an excursion of about 10 mm. A roentgenogram is then taken to corroborate the positioning of the gastric and esophageal balloons. Current tubes have radiopaque balloons which can be visualized on an x-ray film.

Next, the gastric contents are aspirated again and, if necessary, the stomach irrigated with saline solution until all the blood has been removed. When the tube has been positioned and inflated properly and the bleeding continues as indicated by the character of the gastric aspirate, this indicates that the bleeding is due either to a peptic ulcer or to high gastric varices. To rule out the possibility of the latter, the stomach balloon is progressively inflated with 50-cc. increments over 10-to-15-minute periods, with the gastric aspirate again being checked at each interval until a total of 300 cc. of air has been introduced into the gastric balloon.

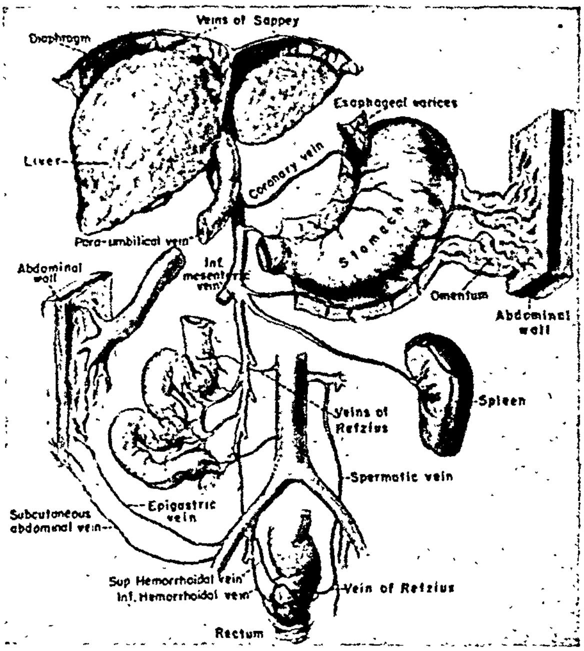

Fig. 1.—Retroperitoneal collateral circulation; natural anastomotic shunts by which venous blood may bypass liver and travel from portal bed to systemic venous system.

At this point, if fresh blood is obtained from the stomach, it may be assumed that a bleeding peptic ulcer is the cause of the hemorrhage, and appropriate treatment instituted. If the patient is known to be cirrhotic, an emergency laparotomy is probably indicated if he can possibly stand the procedure, as continued hemorrhage into the gastrointestinal tract is a lethal complication in cirrhosis. However, let us assume that the bleeding is controlled by the Sengstaken tube or, at any rate, that the bleeding has ceased. This may be coincidence or it may be due to effective compression by the tube.

To digress briefly—are there any other diagnostic methods of accuracy in determining the source of upper gastrointestinal bleeding? Direct esophagoscopy in the presence of massive esophageal bleeding is difficult, dangerous, and unrewarding. Roentgenographic visualization of the terminal part of the esophagus and stomach in the presence of massive hemorrhage is also time-consuming and frequently unsatisfactory although not as dangerous as it was formerly believed to be. In the presence of shock, it is safer not to attempt either method. Sulfobromophthalein excretion test results and estimation of prothrombin time are also frequently unreliable.

McDermott,[2] of the Massachusetts General Hospital, has advocated a fairly simple quantitative test for blood ammonia levels as an emergency procedure. The normal blood ammonia level is 40 to 60 mcg. of ammonia nitrogen per 100 ml. When gastrointestinal bleeding occurs, ammonia is released into the portal circulation through the metabolic activity of intestinal micro-organisms. This ammonia is detoxified by the normal liver. However, in the cirrhotic patient, the deamination process breaks down and large quantities of ammonia appear in the circulating peripheral blood. McDermott's quantitative test will indicate significantly elevated levels in the range of 100 to 120 mcg.

The reliability of the blood ammonia level as a diagnostic aid for bleeding esophageal varices [3] is found wanting in three situations: 1. The patient with advanced cirrhosis and impaired liver function, who is bleeding from a concomitant peptic ulcer. In this situation the blood ammonia level will rise even if the patient is not bleeding from varices. In fact he may not even have varices, as only 50% of cirrhotic persons will ever form them. 2. When the bleeding is too recent to allow the intestinal bacteria time to produce sufficient ammonia to raise the peripheral blood ammonia levels. This can occur within the first two hours after a hemorrhage. 3. The prior use of intestinal antiseptics. In this case the patient may bleed profusely from esophageal varices, but if there are no ammonia-forming bacteria in the intestine the blood ammonia levels will remain approximately normal. Due to the instability of the reagents, plus the ease of contamination by extraneous sources of ammonia, this test has proved unsatisfactory in our institution.

Balloon Tamponage

In my early experience with the Sengstaken tube, I applied traction, placed a plug of foam rubber into the external nares, and then taped the tube to the foam rubber and to the skin of the nose and cheek. Since considerable traction is necessary to control the hemorrhage and to prevent the esophageal balloon from herniating into the stomach, pressure on the external nares over a period of one to three days has caused an actual slough, and this technique has had to be abandoned, as the resulting deformity can be most disfiguring and difficult to correct.

Rousselot, of St. Vincent's Hospital in New York, who has been interested in the surgical treatment of cirrhosis for many years, has devised a rather complicated apparatus which consists of a molded mask which fits the bony contours of the face and exerts traction on the tube.[4] There is a clever electronic monitoring device which is attached to the tube outlets and a system of alarm bells, buzzers, and lights, which is supposed to alert the nurse and the house staff of any fluctuations in the varying pressures that are exerted on the orifices of the tube. This is subject, of course, to the vagaries of all electronic systems and in addition depends on the budget of the institution and the ability of the service staff to purchase and to keep such an apparatus in good working condition, plus the type of clinical material which will guarantee the frequent use of the apparatus, so that the hospital personnel can be trained in its application.

Although our group treats many patients with bleeding varices, we have felt that a simpler system of monitoring is more dependable and economical. An ordinary catcher's mask applied to the face, to which the tube is attached after a rather severe degree of traction has been applied, is perfectly satisfactory. It must be remembered that when the esophageal balloon is inflated the patient is unable to swallow saliva and must expectorate it if he is conscious; if he is deeply sedated (as most patients are) or in coma, almost constant suction by a nurse who is skilled in tracheal aspiration is necessary in order to prevent aspiration pneumonia, which is one of the common causes of death in esophageal bleeding.

How long should one maintain tamponage? This is a difficult question to answer, and experienced clinicians give a variety of opinions ranging from six hours to three weeks. Linton[5] who has devised his own modification of the Sengstaken tube, which consists essentially of a reinforcement of the distal end of the esophageal balloon to prevent herniation into the stomach, advocates immediate placement of the balloon in the emergency ward and immediate preparation of the patient for transesophageal transthoracic ligation of the bleeding varices, as soon as sufficient blood is obtained, typed, and crossmatched. Blakemore,[6] on the other hand, advocates almost indefinite compression with the balloon, meanwhile preparing the patient for an elective portacaval shunt.

I have followed a course somewhat different from either of these two.[3] Tamponage for a longer period than 48 to 72 hours at an absolute maximum produces an esophagus which is bulky, edematous, and indurated and which responds most ungratefully to any type of surgical manipulation. Transesophageal ligation of varices after this period becomes extremely hazardous, because incisions made into the esophagus after prolonged tamponage have a pronounced tendency to disrupt and produce a fatal mediastinitis and/or empyema. Any direct attack on the varices is performed at a time when the liver function is at its poorest and the mortality from this purely palliative procedure is apt to be higher than one would consider desirable. Furthermore, such a procedure can be considered only preliminary to the subsequent definitive shunt construction which in itself (even in elective cases) carries a respectable mortality.

To sum up this aspect of treatment, it is only fair to say that the use of the tube alone requires constant nursing care, the ever-present hazard of aspiration pneumonia, and constant compression of the esophageal wall, which produces an unfavorable situation for possible transesophageal ligation of varices.

Techniques of Direct Ligation

Transthoracic transesophageal ligation of varices is an operation of some magnitude,[7] particularly in a depleted patient with poor hepatic reserve, especially if it has been preceded by a long period of esophageal tamponage. An additional consideration in such surgery is that, in case of a mistake in diagnosis, it is perfectly possible that a patient may actually be bleeding from a duodenal ulcer which would be missed completely in a transthoracic approach.

Accordingly, it is probably good practice, particularly in the hands of a surgeon who has not had much thoracic surgical experience, to approach the varices transabdominally. A midline epigastric incision, with resection of the xiphoid process if necessary, can result in attainment of good visualization of the cardia of the stomach through a gastrotomy incision as well as an opportunity to explore the stomach and duodenum for a possible peptic ulcer, gastritis, or gastric varices. By placing a 14-in. rubber-shod Scudder clamp across the stomach and gastrocolic and gastrohepatic ligaments, complete control of the collaterals can be obtained and any esophageal bleeding greatly reduced or completely controlled. By division of the triangular ligament of the liver and the phrenoesophageal ligament, the lower end of the esophagus can be mobilized somewhat. The esophagus is not an organ which can be elongated longitudinally to any extent, but, with sufficient mobilization, the distal end can be visualized. A sterile bivalve anoscope can be inserted through a high gastrotomy incision, the lower end of the esophagus visualized, and varices sutured. Three columns are usually present, and an over-and-over running mattress suture of 000 chromic catgut will control the situation adequately.

If bleeding is controlled by use of the Sengstaken tube, the esophageal balloon is deflated in 24 hours.[7] If bleeding recurs, the balloon is reinflated, fresh whole blood is obtained, and the patient is prepared for surgery. If, after another 24 hours of compression, on release of the bag the bleeding recurs, the patient is taken to surgery and, either through a transabdominal or transthoracic incision, depending on the circumstances in the particular case, the varices are ligated. During the period the balloon is inflated 1 Gm. of neomycin is administered every four hours and purgatives (2 oz. of magnesium sulfate) are given through the tube; these preparations and colonic irrigations are given in an attempt to flush out the blood in the intestinal tract. If there is any sign of impending coma or of progressive ammonia intoxication, 40 Gm. of arginine in 400 cc. of dextrose is administered; this treatment is repeated two to four times in 24 hours.

Fresh whole blood replacement in plastic bags is, of course, extremely important, and in patients who do not exhibit ammonia intoxication it frequently becomes necessary to employ heavy sedation. The sedative of choice is paraldehyde, administered either through the tube or rectally. Barbiturates must be used cautiously, as they are detoxified in the liver, and if this organ is too badly damaged they may circulate in the blood stream indefinitely. Vitamin K is administered intramuscularly.

Emergency portacaval shunt has been advocated in this situation, particularly if the bleeding is not controlled by the tube.[8] The mortality for this procedure (performed as an emergency) is extremely high; therefore the procedure should not be used in the average institution or by the average surgeon who is not completely familiar with it.

Definitive Management

What is the proper course of action after emergency ligation of varices? This procedure must be used as a policy of expediency and not as a definitive measure. Some patients have been known to rebleed from esophageal varices within six weeks after emergency ligation.[5] Therefore, it is desirable to retain such patients in the hospital for a period of three to six weeks after emergency ligation of varices and to prepare them for definitive shunt construction as soon as their condition will warrant such a procedure. Linton's criteria for shunt surgery represent an ideal which we find all too seldom in the average hospital practice. Our group has attempted to screen all candidates on a slightly different basis and thus far has had a zero surgical mortality in a series of 19 cases of portacaval and splenorenal shunts done at the Kaiser Foundation hospitals in San Francisco and the Northern California area. We will not perform a shunt on a patient who is jaundiced or who manifests gross ammonia intoxication clinically.[3]

However, we have had a number of patients who have recovered from jaundice and/or hepatic coma by the use of arginine and intensive medical care and who have then been subjected to shunt surgery with a successful outcome. It is desirable that the patient have positive protein balance, with a serum albumin level above 3 Gm.%, absence of ascites, a prothrombin time of more than 50%, and a normal sulfobromophthalein value. Linton's criteria (see table) demonstrate persons who are ideal candidates for shunt surgery, and, as can be seen from Linton's figures, the procedure carries a low mortality for this group.[9] However, few patients fulfill these criteria, and one may justifiably ask if they would not do just as well without surgery. Most of our candidates for shunt surgery have gross clinical ascites, a serum albumin level of less than 3 Gm.%, and a prothrombin time of less than 50%. Because many of these candidates have had repeated episodes of bleeding and have demonstrated that their livers have had sufficient regenerative capacity to enable them to survive these episodes, we will operate on most patients who have a clear sensorium, who are gainfully employed, who understand the nature of the problem of alcoholism and wish to be rehabilitated, and who are not jaundiced.[10]

*Correlation of Liver Function Test Results with Postoperative Deaths in Seventy-five Patients, Massachusetts General Hospital, 1945-1951**

Test	Result of Test	Survivals, No.	Deaths, No.	Mortality, %
Serum albumin	Less than 3 Gm.%	1	5	83
	More than 3 Gm.%	57	6	9
Ascites	Failed to respond to medical treatment	5	4	44
	Disappeared on medical treatment	5	2	28
	None	54	5	8
Prothrombin time (above normal)	More than 4 sec.	25	9	27
	Less than 4 sec.	37	2	5
Cephalin flocculation	3+ to 4+	25	11	31
	1+ to 2+	39	0	0
Sulfobromophthalein retention (5 mg./kg.)	More than 10%	39	9	19
	Less than 10%	22	0	0
Van den Bergh	More than 1.0	30	6	17
Bilirubin (mg./100 cc.)	Less than 1.0	32	4	11

* Data from Linton, R. R.: Diseases of Liver, edited by L. Schiff, Philadelphia, J. B. Lippincott Company, 1956, p. 223.

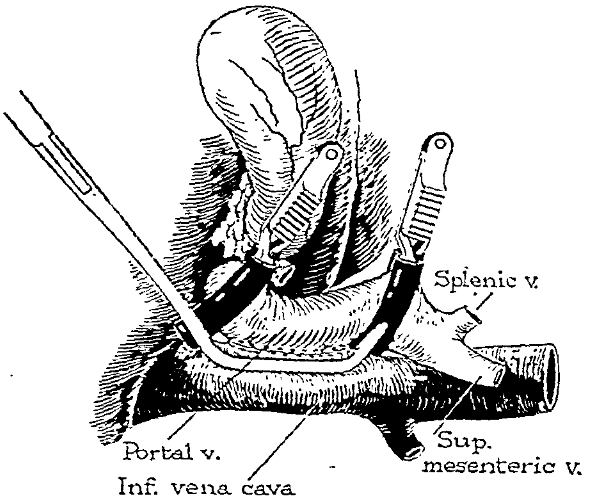

Fig. 2.—Side-to-side portacaval shunt.

What type of shunt should one use? A splenorenal shunt is the most physiological and, in some respects, the safest to perform. However, it can be a difficult and trying operation. Thrombosis is four times as frequent as in a portacaval shunt,[10A] and portal pressure is not affected as positively or as permanently. The side-to-side and double shunts (fig. 2 and 3) have some theoretical physiological advantages in that the entire blood flow from the splanchnic bed to the liver is not diverted into the vena cava.[11] However, it is questionable whether this is actually the case in a patient with advanced

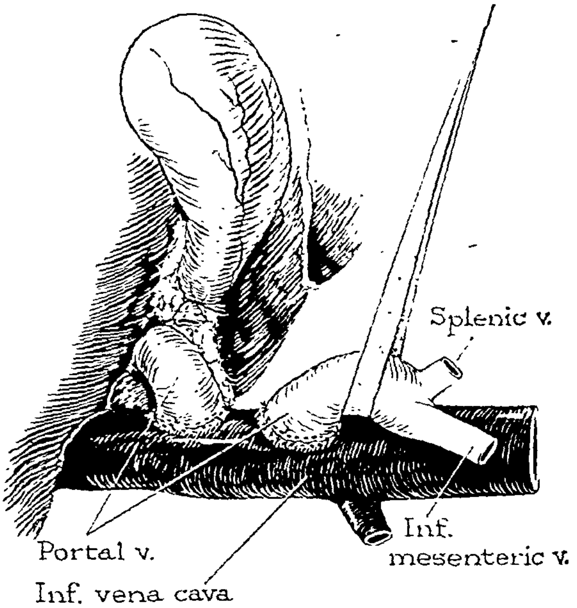

Fig. 3.—Double portacaval shunt.

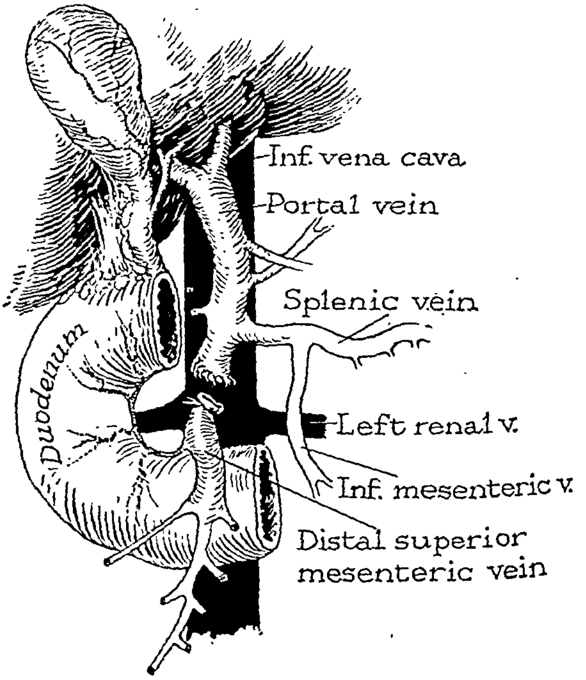

Fig. 4.—Superior mesenteric shunt.

cirrhosis and severe portal hypertension.[1] It is probable that there is an actual reversal of blood flow from the liver into the inferior vena cava in the side-to-side shunt and almost certainly in the double shunt. Furthermore, the side-to-side shunt tends to produce eddy currents and lamination of blood, which increase the risk of thrombosis at the anastomotic site. For these reasons and several others we employ the end-to-side shunt when feasible.

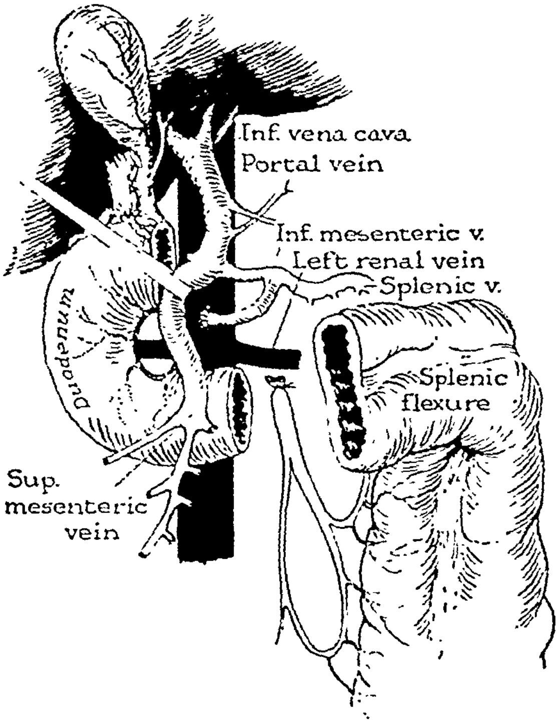

Fig. 5.—Inferior mesenteric shunt.

Situations will arise in dealing with extrahepatic block wherein the vessel to be anastomosed is less than 1 cm. in diameter. This will occur in an attempt to perform a shunt in a patient who is less than 10 years of age, the patient who does not have splenomegaly, or the patient who has had a previous splenectomy. Various types of minor shunt procedures have been performed in the past (fig. 4, 5, and 6). Due to the small size of the vein and the low pressure gradient, such shunts will almost uniformly become occluded. Percutaneous splenoportography is a reasonably safe and accurate guide as to the size of the splenic vein and should be performed (prior to shunt surgery) only in a patient with a palpable spleen of 150 Gm. or more. Patients with bleeding varices due to extrahepatic block who have a splenic vein less than 1 cm. in diameter had best be treated by transesophageal ligation of the varices, which can be repeated if necessary until the patient is old enough to have a splenic vein of sufficient caliber to remain patent.[10b]

If the bleeding is recurrent and serious or if the patient has had a previous splenectomy, it may then be necessary to resort to a procedure designed to interrupt the collateral vessels between the occluded portal vein and the esophageal plexus. Gastric bisection or distal esophagectomy and proximal gastrectomy have been advocated for this purpose.[12] Such operations carry a respectable mortality and are usually of only temporary benefit, because venous collaterals tend to re-form within a period of 18 months, and recurrent bleeding is apt to ensue. However, one has little else to offer such patients.

Summary and Conclusions

Hemorrhage from esophageal varices is probably a reflection of anatomically undeveloped retroperitoneal collateral vessels. The exact mechanism of bleeding is obscure and cannot be reproduced in experimental animals.

Diagnosis of upper gastrointestinal bleeding is important and may be misleading because of the high incidence of peptic ulcer in patients with cirrhosis. (Twenty-five per cent of our bleeding cirrhotic patients do not bleed from varices but rather from a concomitant peptic ulcer or gastritis.) The best diagnostic and therapeutic tool in emergency situations is the Sengstaken-Blakemore tube. Auxiliary diagnostic measures include sulfobromophthalein determination, blood ammonia level determination and "barium swallow," liver biopsy, and hepatic wedged pressure studies.

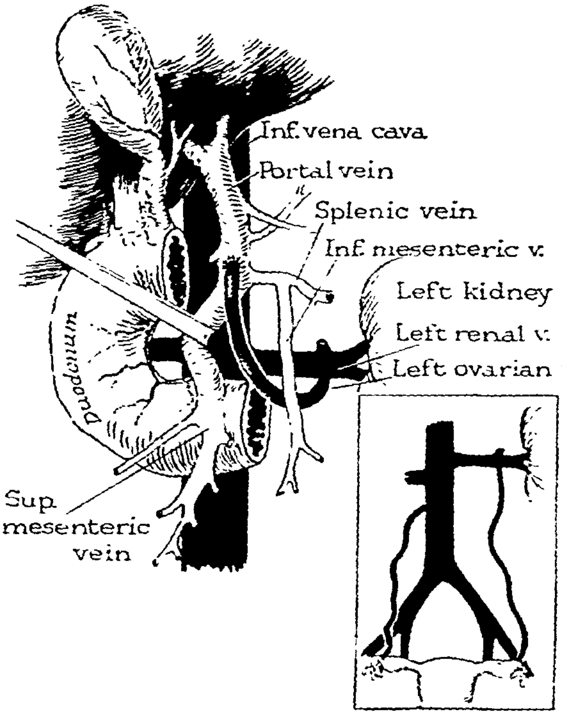

Fig. 6.—Ovarian (or spermatic) shunt.

If the Sengstaken tube fails to control bleeding, emergency laparotomy and gastrotomy is indicated. Bleeding peptic ulcer and gastric or esophageal varices can be controlled through such an incision.

Emergency shunt is not advocated in the usual situations in the average hospital. Elective or urgent portacaval end-to-side shunt is recommended for all patients who have had recurrent bleeding from proved esophageal varices, who are not jaundiced, and who show no signs of ammonia intoxication. Such patients should be brought to the optimum level of hepatic function prior to surgery. Splenorenal shunt is recommended for all those patients with extrahepatic block who have a splenic vein over 1 cm. in diameter.

2425 Geary Blvd.

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EXSTROPHY OF THE BLADDER

REVIEW OF ONE HUNDRED FIFTY-SIX CASES

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The author treated 101 male and 55 female patients who had various congenital defects of the urinary bladder. The defects ranged from mild forms and normal external genitalia to extreme forms and the absence of one or more essential structures, which made it exceedingly difficult for the surgeon to offer the patient any prospect of a socially normal life. Since 1950, ureterointestinal anastomosis and cystectomy have been performed during the first year of the patient's life. Of the 130 patients in this series who underwent ureterosigmoidostomy with cystectomy, 75 were not more than one year old; in the entire series there were six operative deaths (4.6%). Although serious complications after operation have been observed, 100 patients are alive from 1 to 29 years after operation, and valuable knowledge has been accumulated. Recently, ureteroileosigmoidostomy has given gratifying results; of 14 children treated, all but one survived.

Exstrophy of the bladder is one of the most distressing congenital anomalies. It occurs once in every 30,000 to 40,000 births and is more frequent in males than in females, the ratio being approximately four males to one female. My series of 156 patients included 101 males and 55 females.

There are three types of exstrophy of the bladder, (1) superior vesical fissure, (2) inferior vesical fissure, and (3) complete exstrophy. The incomplete types 1 and 2 are rare; in patients with these types the defect in the abdominal wall is relatively slight, and only a small protrusion of the everted superior or inferior part of the bladder is presented. The genitals are normal and the pubes are united. These types of exstrophy are amenable to correction by plastic closure of the bladder and abdominal wall. Three patients in this series had incomplete exstrophy of the bladder.

Type 3, complete exstrophy of the bladder, is the type usually observed. In patients with this condition the anterior wall of the bladder is absent,

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with a fissure of the anterior abdominal wall. In consequence, the entire posterior wall of the bladder protrudes. The mucosa of the bladder is fiery red and exquisitely tender and bleeds readily. The mucocutaneous margins are well defined. As the child becomes older, portions of the exposed bladder assume a grayish color as squamous epithelium replaces the normal cellular structure of the mucosa of the bladder. Usually the ureteral orifices may be detected, because urine intermittently spurts from them. There are diastasis of the rectus muscles and separation of the pubic bones.

In the male patient with type 3 exstrophy of the bladder the penis is usually represented by a rudimentary stump with epispadias and a wide-open urethral meatus exposing the floor of the urethra, the colliculus seminalis, and the bladder neck. The scrotum is smaller than normal and frequently cleft, and cryptorchism generally exists. In this series of 156 patients only one of 101 male patients had a normal penis. In the female patient with type 3 exstrophy of the bladder the clitoris is cleft and the labia minora are widely separated anteriorly, exposing the vagina. Epispadias is usually present.

Coexisting nonurologic and urologic anomalies are frequently observed which may influence the treatment to be instituted. In this series of 156 patients the coexisting nonurologic congenital anomalies included indirect unilateral inguinal hernia (23 patients), bilateral indirect inguinal hernia (18 patients), rectal prolapse (13 patients), hydrocephalus (one patient), spina bifida (5 patients), clubfoot (3 patients), anal stricture (3 patients), harelip (2 patients), cleft palate (2 patients), vaginorectal fistula (2 patients), imperforate anus (3 patients), double vagina and bicornate uterus (one patient), supernumerary arm and leg and two right hands (one patient), absence of vagina (2 patients), and absence of rectus muscles (one patient).

The coexisting urologic anomalies included epispadias in all of the male children except the boy with the normal penis; cryptorchism, in which the testes did not descend into the scrotum when the child cried or could not be placed into the scrotum by gentle manipulation with the examining hand (44 patients); complete bifid scrotum (23 patients); reduplication of the ureters (11 patients); bifid penis (6 patients); pseudohermaphroditism (3 patients); cloaca (2 patients); double penis (2 patients); double bladder (1 patient); horseshoe kidney (2 patients); and normal uterus, ovarian tubes, ovaries, and vagina in a child whose mouth scrapings under cytological study indicated a genetic male (one patient). In the female children additional anomalies consisted of cleft clitoris (usually present); vesicorectal fistula (two patients); and vesicovaginorectal fistula (two patients).

The presence of coexisting anomalies does not necessarily mean that surgical intervention is not feasible. In most instances the coexisting anomalies may be corrected by appropriate surgical procedures, and the erstwhile severely handicapped child may be restored to social normalcy. Unless these unfortunate children are given the benefit of surgical treatment about one-half of them will die in early childhood and two-thirds of them will die before attaining 15 years of age.

Prior to 1950 it was generally accepted that surgical intervention for exstrophy of the bladder should be deferred until the child was 5 or 6 years of age. At that time I wrote that ureterointestinal anastomosis and cystectomy should be performed during the first year of life.[1] In a child of that age the kidneys are usually normal, not having been subjected to repeated attacks of pyelonephritis, and the ureters are of normal caliber. In the absence of dilatation of the ureters their implantation into the rectosigmoid is rendered less technically difficult. The end-results secured after ureterointestinal anastomosis in infants justify recommending the operative procedure at this period of the child's life.

Ureterosigmoidostomy with cystectomy was performed in 130 of the 156 patients with exstrophy of the bladder. Their ages at the time of operation were as follows: up to and including 1 year, 75 patients; 2 to 4 years, 25 patients; 5 to 9 years, 14 patients; 10 to 14 years, 5 patients; 15 to 19 years, 1 patient; 20 to 29 years, 7 patients; and 30 to 39 years, 7 patients. The operative procedure employed was a modification of the Coffey I operation (ureterosigmoidostomy); with a mucosa-to-mucosa anastomosis between the rectosigmoid and the ureter. There were 6 operative deaths in 130 patients, an operative mortality of 4.6%.

Recently, in collaboration with Turnbull,[2] I reported a new operation called "ureteroileosigmoidostomy," which has been giving good end-results. In most of the patients in whom this procedure has been employed a ureterointestinal anastomosis was constructed previously, either by me or by other surgeons. Subsequent dilatation of the ureters necessitated surgical intervention for the relief of ureteral obstruction. The operation has been performed in 14 children; one patient died in the hospital after operation.

Although the end-results secured by ureteroileosigmoidostomy and cystectomy are gratifying, insufficient time has elapsed since the 14 operations were performed to warrant drawing definite conclusions at this time.

A plastic procedure, with reconstruction of the bladder and the urethra, was employed in five patients. One patient died of acute pyelonephritis after operation; subsequently two patients in whom the operative procedure was a failure required ureterointestinal anastomosis. Two girls are living and well six and nine years, respectively, after operation. Both of these girls have mild stress incontinence.

Of the 130 patients who underwent ureterosigmoidostomy and cystectomy for exstrophy of the bladder 36 had major operative or immediately postoperative complications. These included acute pyelonephritis, 13 patients; wound infection, 5; evisceration, 5; anuria, 3; strangulated inguinal hernia, 2; otitis media, 2; leakage (left ureterosigmoidostomy necessitating nephrostomy), 2; postoperative pneumonia, 2; acute pyelonephritis (fatal), 2; and cardiac arrest (fatal), 2.

Of the 124 patients who underwent ureterosigmoidostomy 99 had delayed major complications. Hyperchloremic acidosis of varying severity occurred in 48 patients, pyelonephritis in 36, uremia in 5, renal calculus in 4, strangulated inguinal hernia in 3, epidermoid carcinoma of the remnant of the bladder in one patient, partial intestinal obstruction (adhesions) in 1, and intussusception of the jejunum in 1.

Of the 124 patients who underwent ureterosigmoidostomy for exstrophy of the bladder 16 died postoperatively; the range of survival was from less than one year to nearly eight years. The causes of deaths, number of patients, and length of survival are as follows: uremia, less than one year, one patient; pyelonephritis and uremia, less than one year, two patients; pneumonia, less than one year, one patient; pertussis and pneumonia, less than two years, one patient; pyelonephritis, less than two years, one patient; uremia, less than two years, one patient; cardiac arrest (at another hospital, during repair of epispadias), less than three years, one patient; pyelonephritis, less than five years, two patients; atelectasis, pulmonary congestion, and acute splenitis, less than six years, one patient; pneumonia and uremia, less than seven years, one patient; anuria, after lysis of adhesions, and intestinal obstruction, less than one year, one patient; acute appendicitis, less than three years, one patient; acute pyelonephritis with bilateral cortical abscesses found at autopsy, less than eight years, two patients.

From the review of the records of the 156 patients with exstrophy of the bladder under my care the surgical procedure that I prefer, at the present time, is ureterosigmoidostomy. One hundred eight patients are living for from 1 to 29 years after operation, and the findings in the postoperative roentgenograms are normal (both ureters and kidneys) in 41.4% of the patients. Should ureteral obstruction and dilatation ensue, necessitating surgical intervention at a later date, the ureters may be retrieved from the intestine and a ureteroileosigmoidostomy may be performed.

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FAMILIAL ESOPHAGEAL EPIPHRENAL DIVERTICULA

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and
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Demonstration of multiple epiphrenal diverticula in a male parent and two of his children, with tracheoesophageal fistula found at birth in a grandchild, lends strong support to the concept that familial genetic defect is a possible etiological factor. The diverticula in these reported cases were found to extend over the entire lower esophageal segment. Acute complications had not been recorded in the parent or children. Evidence indicates that such patients should be treated conservatively.

Multiple epiphrenal diverticula are rare, and no etiological basis has been definitely established. The occurrence of multiple epiphrenal diverticula in various members of different generations of the same family has not previously been reported. Such an occurrence appears significant in that it tends to establish a definite genetic factor as a probable etiological factor in this anomaly. The purpose of this paper is to demonstrate the apparent action of a genetic factor in one family by the demonstration of multiple epiphrenal diverticula occurring in father, son, and daughter, and of a tracheoesophageal fistula at birth in a grandchild, offspring of a

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second daughter who was not examined. It is thought that these findings are worthy of reporting as a new clinical type.

Incidence and History

Epiphrenal diverticula are a relative rarity. In one study [1] a review of 20,000 "barium swallows," without regard to the reason for the examination, only three epiphrenal diverticula were discovered. A review of the literature reveals that a total of only 126 cases were reported prior to 1952.[2] Since that time the number of case reports has more than tripled. Approximately 3% of all esophageal diverticula are epiphrenal.[3] More than one diverticulum in the same patient is indeed a rarity.

The first accurate description of the clinical symptoms and anatomic findings in a case of epiphrenal esophageal diverticulum was made by Deguise in 1804. Reitzinstein [4] is credited with the first roentgenologic demonstration of such lesions in 1898. Enderlen [5] performed the first successful surgical correction of one such diverticulum in 1910. All of the listed reported cases were of large, single diverticula.

Etiology

The etiological basis of epiphrenal diverticula has been attributed to various factors. Many investigators [6] have felt that epiphrenal diverticula are congenital. Partial agenesis of esophageal musculature with relatively thinly spread muscle fibers has been described.[6c] Solis-Cohen and associates [6b] have reported a single case in which was found one diverticulum of the hypopharynx, two additional diverticula at the level of the aortic arch, and one additional diverticulum at the epiphrenal level. This patient demonstrated a markedly weakened esophageal muscular wall but gave no history suggesting an acquired condition which might possibly have produced this weakness. Other authors [7] have described patients with similar but less marked hypoplasia of the muscular wall. In some cases epithelial thinning has been observed microscopically but no other findings of significance were found. Palmer [6d] has stated that a congenital neuromotor dysfunction was the initiating factor involved and that the enlargement of a diverticular sac was secondary to normal pulsive forces exerted during swallowing.

The pulsive force is greatly increased in cardiospasm,[2] and this condition must be considered as an etiological agent. Vinson [8] found 8 cases of cardiospasm among 40 cases of proved epiphrenal diverticula. Some authors [9] have felt that the presence of the diverticulum may have been the initiating factor in producing the cardiospasm. Only a small percentage of the persons suffering from cardiospasm have epiphrenal diverticula.[10]

Report of Cases

The following case presentations, we believe, establish a familial or genetic factor as the probable etiological basis for multiple epiphrenal diverticula in the family described.

Case 1.—A 72-year-old man gave a history covering a period of 30 years, during which he had had intermittent pain with swallowing, occasional choking attacks with vomiting of recently ingested food, and frequently associated attacks of violent singultus. Heartburn was never a symptom. The pain and spasms described were usually initiated by the act of deglutition and lasted from 10 to 15 seconds. This patient had no brothers or sisters and was not aware of any history of dysphagia in his parents. Barium esophagrams revealed multiple epiphrenal diverticula (fig. 1), which on fluoroscopy were noted to contract to expel the barium back into the esophageal lumen.

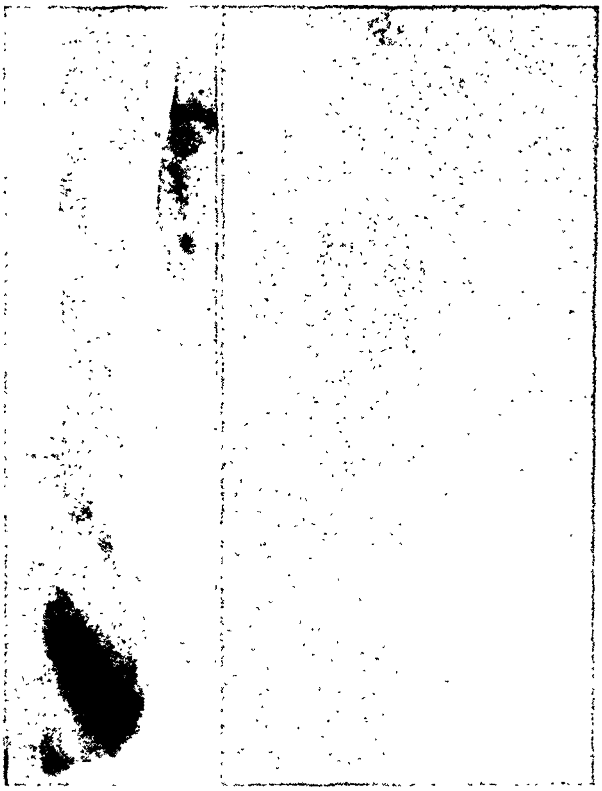

Fig. 1. (case 1).—*Left,* esophagram showing multiple epiphrenal diverticula. *Right,* esophagram showing, in detail, variation in contractile action of epiphrenal diverticula.

Case 2.—A 38-year-old son of the patient in case 1 was first seen after a complete esophageal obstruction from a bolus of meat (fig. 2, *left*). For a period of 16 years previously he had had symptoms of heartburn and painful "spasms of the esophagus" which could often be initiated by simply smelling food. A similar episode of complete esophageal obstruction by a bolus of meat occurred just one year previous to the present admission. Additional history revealed the presence of a duodenal ulcer. Results of physical examination were negative except for cryptorchism bilaterally. The esophageal obstruction was relieved by administration of papaya and irrigation. A subsequent barium esophagram revealed multiple epiphrenal diverticula which were also capable of contraction and on fluoroscopy were noted to expel the barium back into the esophageal lumen (fig. 2, *right*). An incidental finding on this examination was a diverticulum of the duodenum. This patient had no children.

CASE 3.—A 43-year-old daughter of the patient in case 1 gave a history of dysphagia for the preceding 10 years and recalled having had more than three attacks of esophageal obstruction during that time. When eating fast (or gulping her food, as was the family habit) she often noted that a bolus of food would seem to stop in the middle of the esophagus, after which cramping pains would occur and persist until a few seconds later when the bolus would "turn loose and go on down into the stomach." Eating dry foods would always give a "choking sensation." An esophagram disclosed multiple epiphrenal diverticula, which on fluoroscopy would fill and empty with contractile motion. A son, aged 10 years, and two daughters, aged 6 and 15 years, were totally asymptomatic, and normal barium esophagrams were obtained.

Fig. 2 (case 2).—*Left*, complete esophageal obstruction shown at initial examination. *Right*, esophagram showing multiple epiphrenal diverticula.

CASE 4.—Another daughter of the patient in case 1 apparently was asymptomatic and would not submit to roentgenographic examination. Her daughter (granddaughter of the patient in case 1) had a tracheoesophageal fistula at birth; it was surgically repaired shortly thereafter, and the patient was asymptomatic postoperatively. She is now in her late teens and has remained asymptomatic throughout her life. The tracheoesophageal fistula in this case was the most common variety with the blind upper esophageal pouch and the lower esophageal segment attached to the trachea just above the carina. There were no other congenital anomalies present. There are no other children in this family.

Comment

The occurrence of multiple epiphrenal esophageal diverticula in three members of the same family representing two generations and the further unusual finding of a tracheoesophageal fistula in the third generation surely lends strong support to familial genetic defect as a possible etiological factor in the development of such pathological entities. This limited study further suggests that the etiological factors in multiple diverticula probably differ from factors in development of a single diverticulum. The fact that dysphagia did not develop until several years after birth in those with diverticula suggests that there may be congenital weakness of the esophageal wall and that the stress of daily living subsequently leads to the development of multiple diverticula in these areas. All the members of this family are of the rather "nervous" type and have the habit of eating rapidly. Gulping of food may have contributed to, but is not sufficient cause per se, for development of the multiple diverticula.

Generally speaking, asymptomatic epiphrenal diverticula require no treatment. If the diverticula become large enough to lead to rotation into a dependent position and so cause displacement of the esophagus,[11] surgical therapy is then necessary. Hydrostatic dilatation usually produces only temporary symptomatic relief for the patient with a large single epiphrenal diverticulum.[12]

A review of the presented cases shows that first patient attained the age of 72 years, with only moderately pronounced symptoms over a period of 30 years and without development of any severe complication. Since the diverticula in these cases were found to extend over the entire lower esophageal segment, moderately extensive excision would be necessary to remove the involved segment if surgical therapy were attempted. These considerations lead us to believe that similar cases of epiphrenal diverticula should be treated conservatively.

Summary

Three patients, representing two generations in a single family, had multiple epiphrenal diverticula. A member of the third generation had a tracheoesophageal fistula. Conservative management is recommended for this syndrome.

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INNER-EAR MECHANICS AND DEAFNESS

SPECIAL CONSIDERATION OF MÉNIÈRE'S SYNDROME

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Intensive study was made of the changes in the inner ear of a woman who died of other causes after suffering from Ménière's syndrome for four years. There was evidence that the ductus cochlearis had been overdistended by an excess of endolymph and that its rupture had been followed by partial repair. This would explain the fact that the symptoms had come in spells and that there had been a remission lasting two years. If the underlying process in Ménière's syndrome is overproduction of endolymph in the cochlea, then the logical remedy is either destruction of the cochlea or some other method of reducing the hydrops, rather than the destructive labyrinthotomy which had been contemplated. Destruction of the cochlea produces deafness but would relieve the vertigo, which is the more disabling of the two symptoms.

Once sound vibrations have been introduced into the fluids of the inner ear, either through the forcing movements of the stapes or through bone conduction, there are still two basic processes on which adequate stimulation of the neural elements depends. One of these is a mechanical one, the process whereby the vibrations are transmitted through the fluids and the energy distributed along the basilar membrane so that the sensory cells are appropriately stimulated. The other process is the one by means of which the mechanical vibrations are utilized to produce an electrical form of energy capable of stimulating the nerve fibers. This latter process is the responsibility of the sensory cells.

If either one of these two processes is interfered with, a loss of hearing results. It is easy to imagine how a substance toxic to the sensory cells could be present in the endolymph, resulting in deterioration and eventual death of these cells. It is not so easy to imagine how the mechanical operation of the inner ear can be detrimentally affected.

One set of conditions that may have a mechanical effect on inner-ear sound transmission as well as a toxic effect on the sensory cells is that connected with what has come to be called Ménière's syndrome. The symptoms associated with this entity are those of tinnitus, progressive fluctuating deafness, and periodic attacks of vertigo, nausea, and vomiting. Because these disturbances involve the

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functions of both auditory and nonauditory parts of the labyrinth, it is obvious that the precipitating condition is widespread throughout the inner-ear structures, and the one universal finding in these cases, as observed by Hallpike and Cairns,[1] has been a hydrops of the membranous labyrinth.

Often in the presence of the dilatation of the labyrinthine system brought about by this hydrops the sensory areas have appeared normal. Such observations have led to theories that the hydrops, by increasing the endolymphatic pressure, somehow interferes with the transmission of sound within the inner ear.

Lindsay [2] discussed this possibility and recently Tonndorf [3] showed how increased fluid pressure can affect the behavior of a model resembling the ear. This model contained an enclosed channel, representing the endolymphatic scala, which was included between two other connecting channels containing an opening at each end to represent the perilymphatic scalae. Increased fluid pressure in this system produced changes in the behavior of the vibratory patterns within the model that apparently, to the investigator, were consistent with some of the symptoms associated with Ménière's syndrome.

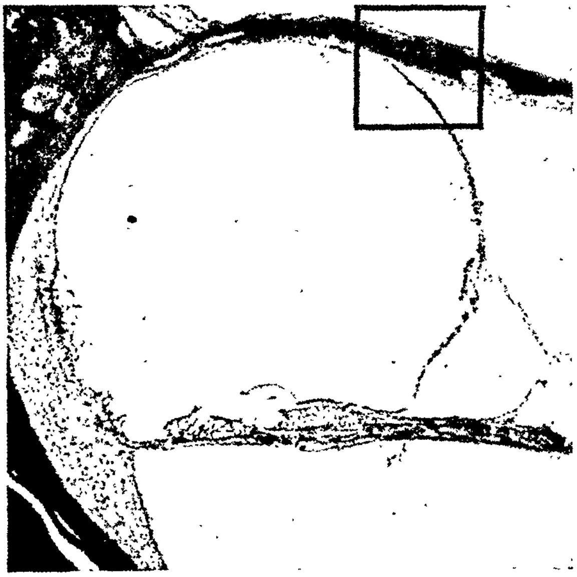

Fig. 1.—Scala media from right cochlea of patient with attacks symptomatic of Ménière's syndrome. Reissner's membrane is greatly distended, and endosteum of scala vestibuli is thickened. No changes in organ of Corti or stria vascularis are apparent, other than those expected by autolysis. Outlined area is shown, enlarged, in figure 5.

One of these symptoms is that of sound distortion. Patients suffering from these symptoms often complain of being able to hear sounds which, when heard, are distorted and uninterpretable. By certain procedures [4] it is possible to determine the level above the threshold at which this distortion becomes just noticeable by a human observer. In patients with Ménière's syndrome the range of hearing between threshold and beginning distortion is much less than in normal patients, but, because of the raised threshold, actually more sound pressure is required to bring on this distortion than in the normal ear. Tonndorf apparently misinterpreted this fact and his model showed that the sound pressure level at which distortion was produced was lowered by increasing fluid pressure. If a model demonstrates an error in one dimension it is doubtful that it can be used as proof in any other dimension. These experiments offer no evidence that hydrops has a mechanical effect on sound transmission.

Other experiments in animals, such as those of Lempert and co-workers [5] and Von Békésy [6], have demonstrated that changes in intralabyrinthine pressure do not have any noticeable effect on the production of cochlear potentials. Because of the lack of direct evidence that increase in endolymphatic pressure can alter the function of the inner ear, and because it is difficult to see how pressure could increase rapidly enough to produce the precipitous attacks of vertigo, tinnitus, and sudden feeling of fulness in the ear, the notion of a toxic effect has found favor. But there is no indication of what the chemical substance involved might be or from where it might arise.

We have recently had the opportunity to process and examine microscopically the temporal bones of a patient who had been suffering from all the classic symptoms of Ménière's syndrome. This patient's symptoms resisted all attempts to relieve them by medical treatment, so the patient was scheduled for a destructive labyrinthotomy. During the anesthetic induction, however, the patient developed a cardiac arrest. Although the heart was resuscitated by massage to a normal beat, the patient developed hyperpyrexia and died 38 hours after the arrest. At autopsy the temporal bones were removed, placed in 20% formol, processed in the usual manner, sectioned at 20μ, and mounted serially for subsequent histological review.

A careful study of the histological changes in these bones suggested, when compared with some recently revealed changes observed in animal temporal bones, a possible cause of the precipitous periodic attacks as well as a possible mechanism determining the course of the disease.

Report of a Case

The patient, a 43-year-old woman, came to University Hospital on July 3, 1956, with the chief complaint of recurrent spells of vertigo, nausea, tinnitus, and deafness of four years' duration. The initial episodes were relieved by medication and a two-year period of remission ensued. In the recent months before admission her spells had become increasingly severe. Three courses of intravenous histamine therapy failed to control her disease.

Objective otolaryngologic examination and general physical examination showed normal findings. Functional examination of the hearing by audiometry revealed results as follows:

	128	256	512	1,024	2,048	4,096	8,192
Left	0	0	5	0	0	20	30
Right	50	50	55	60	60	55	40

Bone conduction with 70 db. of masking revealed the following results:

	512	1,024	2,048
Left			
Right	55	60	50

On July 6, 1956, the patient was scheduled for a destructive labyrinthotomy of the right ear. This was not carried out because of her cardiac arrest and subsequent death, described above.

Histological Findings.—Because of the nature of death and the delay in removal of the temporal bones considerable postmortem autolysis occurred, but these changes were not of such a nature as to change the picture on which the present interpretations were made.

Right Ear: The cochlear duct showed the typical picture (fig. 1) of endolymphatic hydrops as described by Hallpike and Cairns.[1] Reissner's membrane was greatly distended into the scala vestibuli, which was not completely obliterated but contained numerous strands of unsystematized connective tissue. The endosteal lining of the scala vestibuli was thickened. The organ of Corti, external sulcus, spiral prominence, and stria vascularis did not show any changes other than those to be expected with this degree of autolysis, and the basilar membrane appeared in a normal position.

The saccule and utricle showed dilatation as well as changes in the sensory cell area. Figure 2*C* shows the saccule. The membrane on the side opposite the macular area was torn, but this had the appearance of having occurred during processing. There were some changes in the sensory cells, which could have been due to autolysis, except that the saccule on the left side did not show similar changes.

Figure 2*B* shows the utricle of this right side. It is obvious, when the sensory cells of this macula are compared with those of the unaffected side (fig. 2*A*), that changes other than autolysis have taken place. The semicircular canals and each crista appeared normal. The endolymphatic sac had been removed, along with the dura on the posterior side of the petrous bone, and so was not available for study. The duct, however, appeared normal. The cochlear aqueduct also appeared normal.

Left Ear: As nearly as could be determined by careful examination of the sections all structures on this side appeared normal. Figure 3 shows the scala media from this side, which can be compared with figure 1. On this left side Reissner's membrane appeared in its normal position, and the organ of Corti seemed normal.

Figure 2*A* shows the macula of the utricle. The sensory cells, otolithic membrane, and nerve supply appeared normal. There was no distention of the membranous wall as there was in the utricle on the right side.

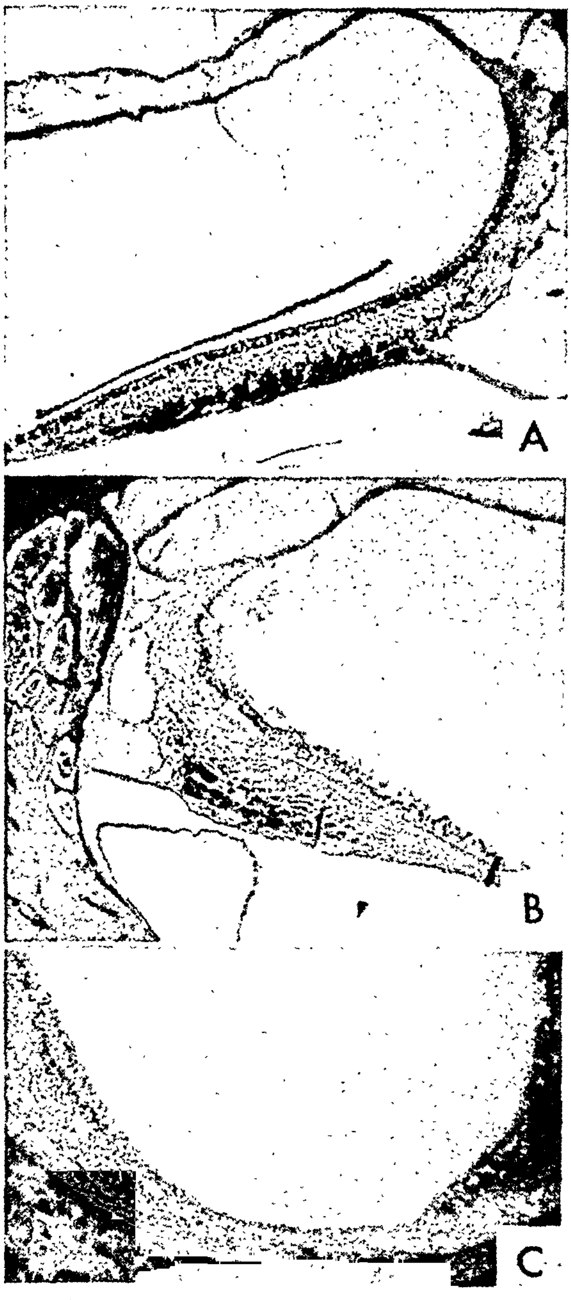

Fig. 2.—*A*, macula utriculi of left ear; *B*, macula utriculi of right ear; *C*, macula sacculi of right ear.

Because of the plane of section on this side it was not possible to obtain a picture of the saccule comparable to that on the right. But from what could be ascertained by careful microscopic examination the macula and membranous walls were normal.

As on the right side the endolymphatic sac had been torn free along with the dura from the posterior side of the petrous bone. The remaining duct, however, appeared normal, as did the cochlear aqueduct.

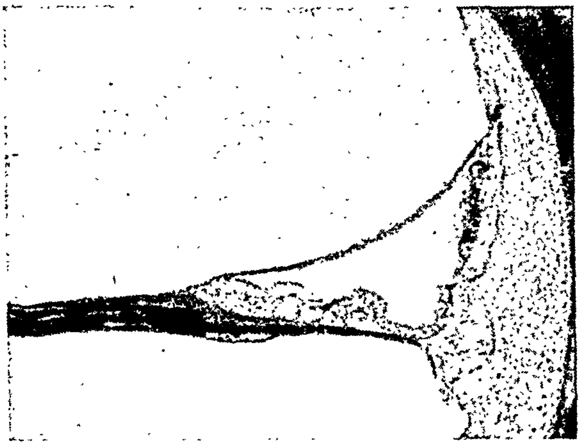

Fig. 3.—Scala media from left cochlea. Changes in organ of Corti and stria vascularis are typical of those to be expected from postmortem autolysis.

Comment

It is quite obvious from this and from most previous reports which describe the histopathological changes in the internal ear that the major occurrence in Ménière's syndrome is a distention of Reissner's membrane along with similar changes in the saccule. It is not so common to find changes in the utricle or in the semicircular canals, although some have been reported, usually in cases of long standing. These observations are no doubt significant in the explanation of the symptoms associated with Ménière's syndrome.

The course of events in this illness usually starts with auditory symptoms. There are tinnitus and some loss of hearing, with a sensation of fulness in the ear. This may persist for some time, with fluctuations in hearing acuity. After various periods this may be followed by vertigo, nausea, and vomiting after or during a period of noticeable tinnitus and depression in hearing. After a period of remission there is usually another attack. These attacks are periodic and sudden in onset and may increase in severity for a time. Eventually hearing becomes permanently depressed and the vertiginous attacks are less violent.

It seems to follow that the initial locus of effects lies in the cochlea, and we suggest that this disease is one primarily involving the pars inferior, i. e., the cochlea and saccule. There is, during the course of the disease, a continuing increase in endolymph content, the reasons for which we have no explanation. This increase occurs in the cochlea and causes Reissner's membrane to bulge into the scala vestibuli, but, because the basilar membrane is stiffer and more firmly anchored, it remains in place. The bulging of Reissner's membrane will equalize the pressures in these early stages, so it is unlikely that any hydrodynamic effect changing sound transmission properties of the inner ear could occur.

As the endolymphatic pressure slowly increases a break in Reissner's membrane eventually occurs, allowing perilymph to mingle with the endolymph in the region of the break. It has been clearly established that the ionic content of endolymph and perilymph are different,[7] and Von Békésy[8] has observed that as he looked at the organ of Corti through Reissner's membrane the cells of this structure appeared as clear oil droplets. When Reissner's membrane is broken these cells take on an opaque appearance and local electrical effects decrease. This contamination of endolymph with perilymph could reasonably account for the loss in hearing.

Since this contamination of endolymph with perilymph alters the performance of the sensory cells by chemical means rather than by mechanical destruction, as in noise overstimulation, it is likely that such changes would not show up by our histological methods.

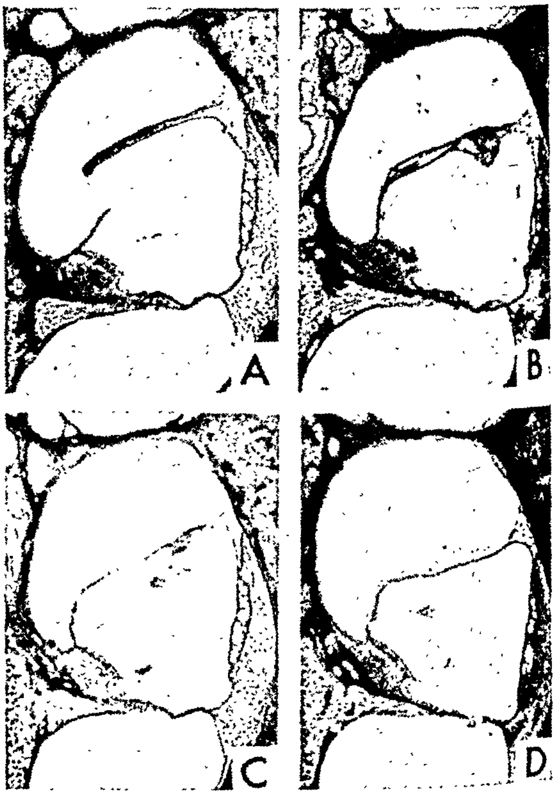

Fig. 4.—Repair of Reissner's membrane seen in guinea pig ear at edge of rupture produced by acoustic overstimulation, which has caused disappearance of organ of Corti. *A*, *B*, *C*, and *D* show progressive changes proceeding from ruptured area to region of healed membrane. Reprinted from Lawrence and Yantis.[9]

After the break in Reissner's membrane the pressures are equalized and the membrane proceeds to repair itself. There is evidence that contamination of endolymph by perilymph does not destroy or alter the function of the entire length of the organ of Corti and that Reissner's membrane can repair itself.

In a study of the effects of acoustic overstimulation on the ears of guinea pigs Lawrence and Yantis[9] subjected a number of animals to noise levels of 136 and 150 db. Two months after this treatment the animals were killed by intravital perfusion and the temporal bones were removed. These were processed, sectioned, and mounted serially for histological study. In most instances the organ of Corti was destroyed over a large area and Reissner's membrane was invariably ruptured throughout the middle region. The fact that this membrane was ruptured would obviously indicate that perilymph had entered the endolymphatic space, and yet, in some regions, especially near the base, the organ of Corti appeared normal histologically and showed a functional capability as determined by recording of the cochlear potentials.

Along the basal and apical margins of the rupture in Reissner's membrane there is evidence of a repair process. Figure 4 shows the nature of this repair. In figure 4*A* the old bit of the membrane can be seen protruding from the limbus. The endosteum from a region above the stria has proliferated, extending into the space between scala media and scala vestibuli, to connect with the remnant in 4*B*. As we move away from the region of rupture this new membrane thins down and in 4*D* appears as a normal Reissner's membrane, except for the fact that it is now attached well above its usual point of attachment at the top of the stria vascularis. In fact, one of the characteristics of a regenerated Reissner's membrane seems to be that it is attached high up on the wall of what was formerly the scala vestibuli. We do not know how far Reissner's membrane will stretch as the supply of endolymph is gradually increased, but we can find evidence in the sections under study that the membrane has broken and reattached itself.

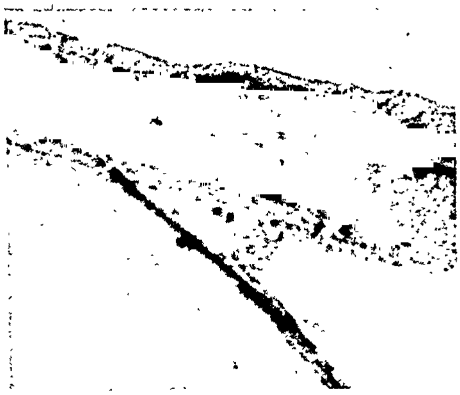

Fig. 5.—Enlargement of area of attachment of Reissner's membrane outlined in figure 1. Membrane apparently has not simply stretched into balloon shape but has ruptured and reattached itself high up on endosteal wall of scala vestibuli.

Figure 5 is a high-power view of the point of attachment of Reissner's membrane of the section of figure 1 which shows that area of enlargement in outline. As seen in figure 5, this point of the membrane appears joined with the endosteum both at its upper extremity and by tissue strands along its course, much as shown for the guinea pig ear in figure 4*D*.

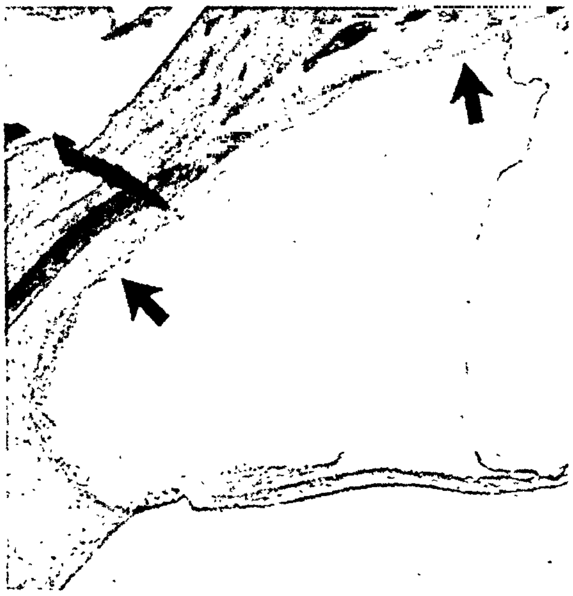

Fig. 6.—Scala media, from more apical turn than that shown in figure 1, of right cochlea. Enlargement of regions indicated by arrows shown in figure 7.

A better picture of this is shown in figures 6 and 7. The scala media in figure 6 shows the usual distention. The two areas of interest are indicated by arrows. Just above the stria vascularis the remaining end of a broken Reissner's membrane can be seen. A high-power view of this is shown in figure 7*B*. At the other end of the membrane a region of attachment can be seen. The membrane, having been stretched before rupturing, lies along the endosteum and shows regions of attachment. A higher-power view of this is shown in figure 7*A*.

This breaking and repair of Reissner's membrane could account for the tinnitus and fluctuating deafness. Presumably, hearing would decrease when the endolymph is contaminated by perilymph and recover to a certain degree as the membrane regenerates.

The source of this excess endolymph is apparently in the scala media, and whether the excess is due to failure of proper drainage or to an excessive production one cannot say; it is apparent, however, that the second seat of influence for this excess fluid will be the saccule. Hallpike and Cairns[1] pointed out that the walls of the utricle

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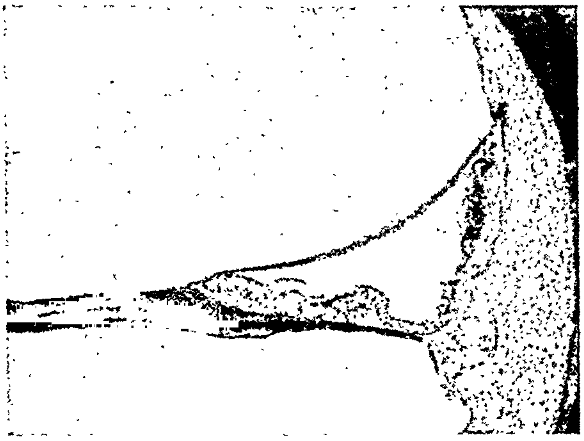

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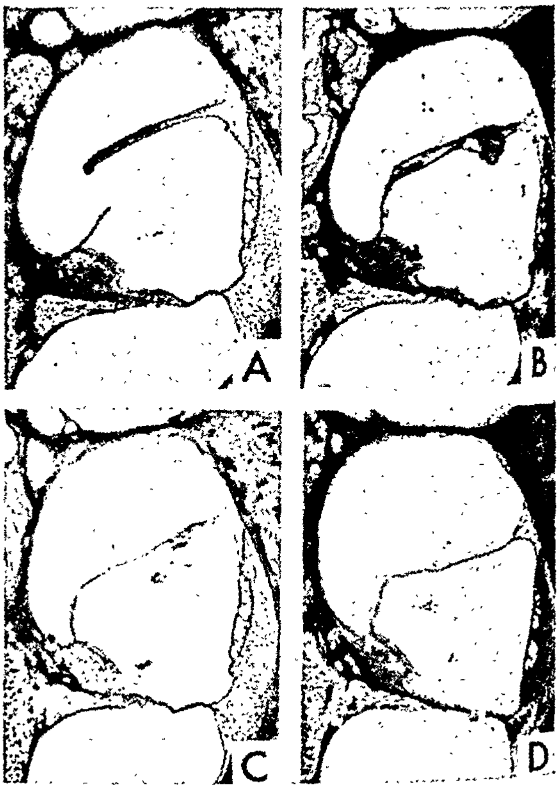

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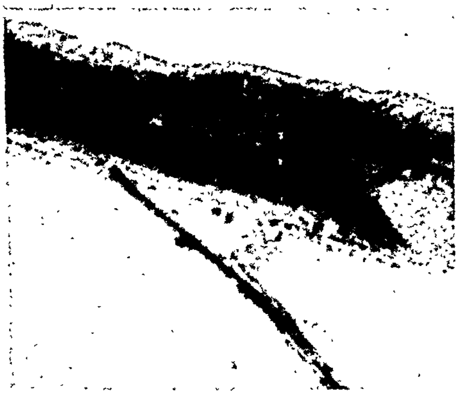

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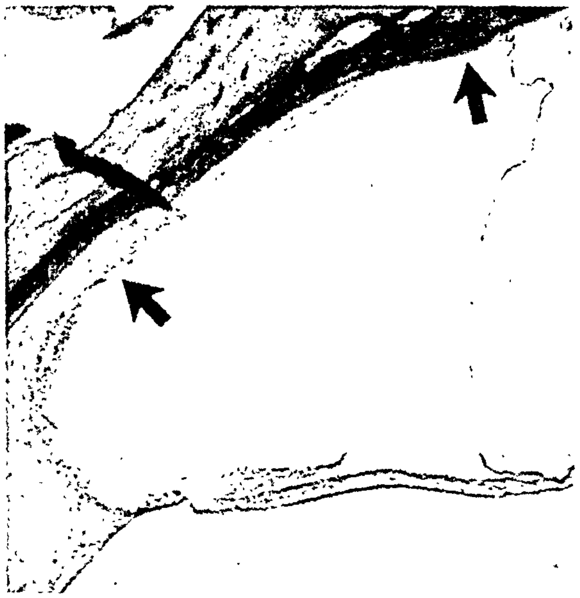

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The source of this excess endolymph is apparently in the scala media, and whether the excess is due to failure of proper drainage or to an excessive production one cannot say; it is apparent, however, that the second seat of influence for this excess fluid will be the saccule. Hallpike and Cairns[1] pointed out that the walls of the utricle are two to three times as thick as those of the saccule, and those of the saccule appear thicker than Reissner's membrane. The increasing endolymphatic pressure acts on the walls of the membranous labyrinth like air in a balloon with thin spots. These thin spots bulge and break first.

The initial attacks of vertigo may well be caused by the effects of perilymph on the saccule, and it may be that this perilymph can enter through the canalis reuniens from the scala media. With a ruptured Reissner's membrane or after several ruptures of this sort the scala vestibuli is practically obliterated and the endolymphatic pressure ruptures the wall of the saccule. We[10] have shown some evidence for saccular involvement in vestibular stimulation, and it is not unreasonable to assume that the strange pattern of vertigo seen in early Ménière's disease is the result of saccular disturbances.

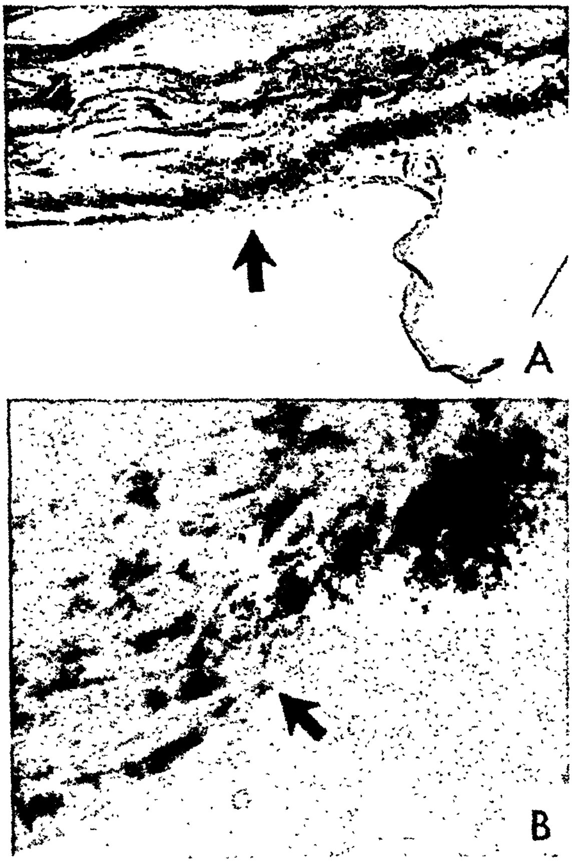

Fig. 7.—*A*, enlargement of upper-arrow area of figure 6. Region of attachment of Reissner's membrane is shown high up on wall of scala media. Membrane has been stretched and lies along endosteum attaching at various points. Arrow indicates region of attachment. *B*, enlargement of lower-arrow area of figure 7. Arrow indicates broken end of Reissner's membrane just above stria vascularis.

As the disease progresses, the utricle and semicircular canals may become involved. By this time hearing is depressed to an unserviceable level, and the patient's vestibular systems have become rebalanced at such a low functional level that the attacks become less severe.

Treatment by means of destructive labyrinthotomy would seem to approach the lesion from the wrong end. Although loss of hearing is a handicap, incapacitating vertigo is more traumatic and these symptoms are thought of first in seeking relief; but since Ménière's syndrome seems to affect initially and primarily the pars inferior it would seem more logical to destroy the cochlea, the source of the excess endolymph. If this were done early enough, before involvement of the pars superior has taken place, it might be possible to relieve the patient of his symptoms, except for deafness, and leave him with two normally functioning vestibular labyrinths.

The ideal solution to the problem of relief of symptoms is, of course, to find the cause of and to prevent hydrops. Failing this, a destructive operation limited to that compartment of the inner ear in which the disease originates would seem to have merit.

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Dr. A. C. Furstenberg granted permission to present this case. Drs. C. F. Derrick and I. M. Blatt assisted in obtaining materials used in this study.

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CLINICAL INTERPRETATION OF TOTAL SERUM AND "PROSTATIC" ACID PHOSPHATASE LEVEL

Howard B. Simon, M.D.
and
Kaare K. Nygaard, M.D., White Plains, N. Y.

A patient who had done well for 10 years after extensive abdominal surgery for malignant disease of the stomach began to show symptoms of metastases, especially to the bones. Laboratory studies of the serum revealed abnormally high levels for alkaline phosphatase, total acid phosphatase, and specific prostatic acid phosphatase, but postmortem examination of the prostate yielded neither gross nor microscopic evidence of prostatic carcinoma. Abnormally high phosphatase levels do not suffice for the diagnosis of prostatic carcinoma.

Since the Gutmans[1] and Barringer and Woodard[2] in 1938 independently observed increased acid phosphatase levels in the serums of certain patients with disseminated prostatic cancer, the measurement of the level of this enzyme has been intimately associated with the diagnosis of this disease. Ensuing reports[3] further confirmed this observation, with elevation of the acid phosphatase level being found in 65 to 85% of patients with demonstrable bony metastases. The usefulness of the test has been restricted, because normal values have been found in a large percentage of cases with widespread metastases[4] and elevated values in only a small percentage of patients with early prostatic carcinoma.[3a] The former observation is believed to be due to certain types of prostatic carcinoma which produce too little phosphatase to be demonstrated in the serum level.

Delory and co-workers[5] in 1951 reported elevation of the total acid phosphatase content in such diverse clinical entities as prostatic hyperplasia; malignancies other than those of the prostate; diseases of the liver, bile ducts, and kidneys; osteitis deformans (Paget's disease); and various other miscellaneous disorders. It became increasingly obvious that for this determination to become clinically useful it would be necessary to refine it so as to identify acid phosphatase from nonprostatic sources. Abul-Fadl and King,[6] in 1949, observed that L-tartrate completely inhibited acid phosphatase extracted directly from surgical specimens of human prostates. Acid phosphatase from erythrocytes was not inhibited. The clinical significance of this observation was not emphasized until 1953 when Fishman and Lerner[7] described a method of determining what they called "prostatic acid phosphatase" by the L-tartrate method, the "prostatic" acid phosphatase being that amount of the total acid phosphatase which was inhibited by L-tartrate.

Three years later Fishman and co-workers[8] reported a study of 91 cases of proved prostatic carcinoma. In this series the prostatic acid phosphatase level was elevated in 87% of untreated and in 81% of treated patients, as compared to elevation of the total acid phosphatase in only 31 and 38% of these groups respectively. These workers felt that only patients with prostatic carcinoma exhibited persistently abnormal values and that elevations in patients with benign prostatic hyperplasia were either transient or indicated an occult carcinoma of the prostate. A study by Mathes and co-workers[9] concluded that "the prostatic acid phosphatase appears to be 30 to 40% more sensitive than total serum acid phosphatase [level]." Cline and co-workers[10] reported a study of 1,106 subjects, concluding that "A male patient with unexplained persistent elevation of serum specific prostatic acid phosphatase [level] above 0.7 units must be considered as possessing prostatic carcinoma until proved otherwise. Elevations above 1.3 units have been observed only in cancer-bearing subjects in this series. No elevations above 1.5 units have been observed in [patients with] any other disorder except prostatic carcinoma."

We had the opportunity to observe, over the course of several months, a patient in whom a persistently high acid phosphatase level was finally proved not to originate from prostatic carcinoma, by postmortem examination. For this reason the present case is reported.

Report of a Case

The patient, a 51-year-old man, was first admitted to the White Plains Hospital on Jan. 16, 1949. A diagnosis of gastric malignancy was established, and on Jan. 18, 1949, a subtotal gastrectomy, omentectomy, gastrojejunostomy, and jejunostomy were performed by one of us (K. K. N.). Evident spread of malignancy at the time of surgery was noted in the regional lymph nodes, and three small nodules were noted in the liver. Pathological ex-

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From the departments of urology and surgery, White Plains Hospital.

amination confirmed the diagnosis of undifferentiated, mucin-producing adenocarcinoma of the stomach, with secondary involvement of the regional lymph nodes (fig. 1).

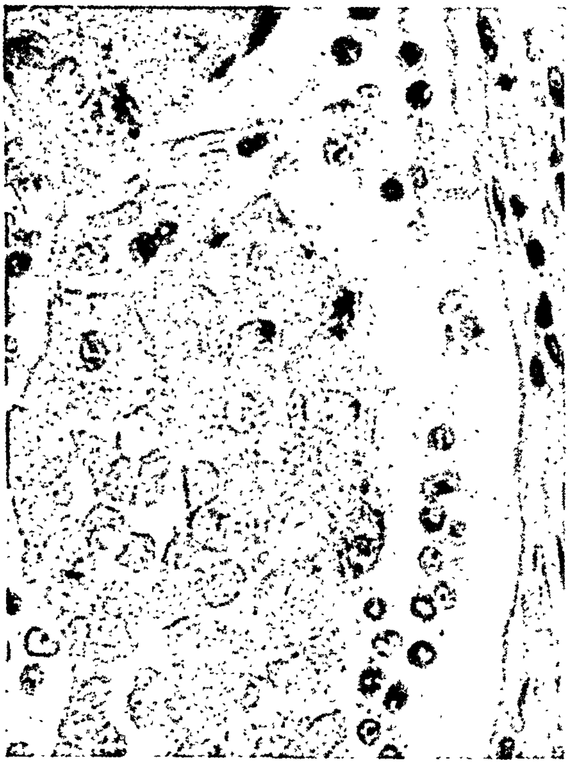

Fig. 1.—Microscopic section of lymph node showing metastatic spread of gastric malignancy, with filling of peripheral sinus by masses of medium-sized undifferentiated round cells having small deeply staining nuclei and cytoplasm that is relatively finely vacuolated. Cells are so closely crowded together that cell outlines are indistinguishable (× 1,050).

The patient did surprisingly well during the ensuing 10 years. He returned to work and remained well, both objectively and subjectively, until April, 1958. He then developed alternating diarrhea and constipation with abdominal cramps, and three months later he returned, complaining of flatulence and left flank pain radiating into the left side of the chest in the posterior axillary line. Pain also developed in his right shoulder and midthoracic spine, poorly relieved by meperidine (Demerol) hydrochloride medication; it became so severe that he was unable to lie flat or to walk, and he had to sleep in a sitting position. He was readmitted to White Plains Hospital on Aug. 4, 1958.

On admission his vital signs were within normal limits. Examination disclosed a 51-year-old man who appeared chronically ill and malnourished. He complained of intense pain in the right shoulder despite recent administration of meperidine. His abdomen was somewhat distended, but the examination was otherwise unremarkable. Rectal examination disclosed a slightly enlarged prostate gland of normal consistency.

Findings of complete blood count and urinalysis were normal. Sedimentation rate was 8 mm. in one hour (Wintrobe), electrophoretic pattern for multiple myeloma was negative, and serum calcium and phosphorus values were within normal limits. His alkaline phosphatase level was 22.2 Bodansky units and total acid phosphatase level, 8.1 Gutman units. A roentgenogram of his chest and right scapula disclosed many small rounded areas of bone destruction scattered throughout the ribs, clavicle, and right scapula, with some suggestion of areas of bone destruction in the vertebral bodies. There was no evidence of pulmonary disease. Roentgenograms of his skull and lumbosacral spine disclosed multiple osteolytic lesions of the cranium (fig. 2), vertebrae, pelvis, and upper ends of the femora.

An electrophoretic pattern for multiple myeloma was again negative, and his urine contained no Bence Jones protein. A biopsy specimen of marrow from the right scapula contained no tumor cells. Repeat serum phosphatase studies again disclosed elevation of the alkaline and acid phosphatase levels (fig. 3).

Estrogen therapy was instituted on an empirical basis, but he continued to require meperidine therapy for relief of pain in the right shoulder, right hip, and back. X-ray therapy to the lower cervical, thoracic, and lumbar vertebrae was instituted. By mid-September the serum phosphatase level had been determined several times and had remained elevated; the total acid phosphatase level varied from 4.7 to 8.1 Gutman units and the "prostatic" acid phosphatase level from 1.8 to 2.3 units. Widespread metastatic gastric carcinoma was considered the most likely diagnosis, but the persistently elevated "prostatic" acid phosphatase level again raised the possibility of prostatic malignancy. Digital rectal examination of the prostate, however, indicated that it was normal, and the bony lesions were osteolytic rather than osteoblastic.

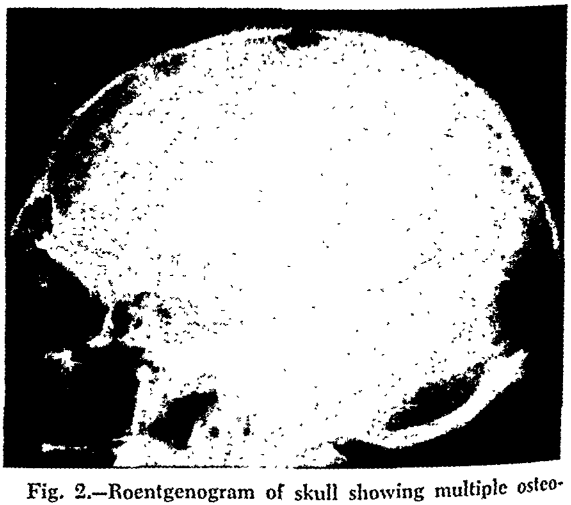

Fig. 2.—Roentgenogram of skull showing multiple osteolytic lesions of cranium.

Since there was little to offer this patient even for palliation, and despite lack of tissue confirmation, biopsy of the prostate being unwarranted in view of the patient's desperate clinical condition, it was decided to perform bilateral orchiectomy and treat the patient as having a possible metastatic prostatic malignancy. This was done and the removed testes exhibited senile atrophy. He had minimal subjective relief after this for a week or so, but severe pain recurred over the right side of the clavicle. X-ray treatment over the clavicle was given, but the pain continued to be severe locally and worsened in other areas generally. Repeat phosphatase studies not only failed to show improvement but, on the contrary, the acid phosphatase levels rose to 10.7 units total and 4.6 units "prostatic," with the alkaline phosphatase level ascending as high as 20.2 Bodansky units. On Oct. 15, 1958, cortisone therapy was instituted on the assumption that orchiectomy, by removing two atrophic testes, had failed to eliminate the principal source of androgen secretion (the adrenal glands) and that "medical adrenalectomy" might be useful. Surprisingly enough, he did experience definite subjective improvement, and his acid phosphatase levels nine days later were decidedly lower, approaching normal (fig. 3). However, on Nov. 5, 1958, he suddenly became paraplegic and severe pain recurred. He developed fluid at both lung bases, rapidly worsened clinically, and finally died four days later.

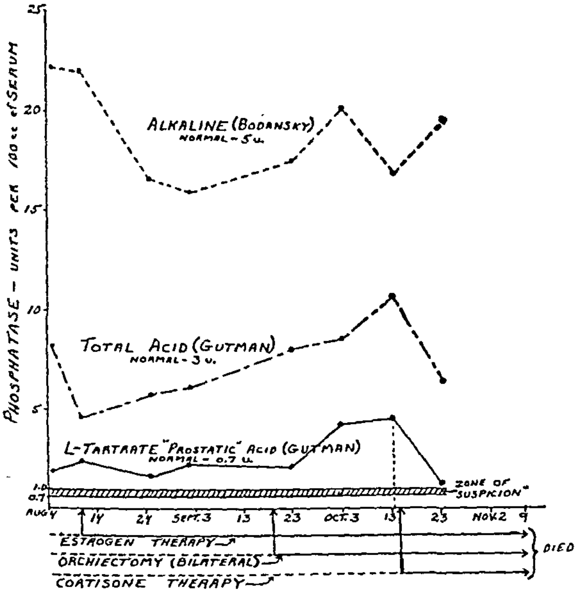

Fig. 3.—Serum phosphatase levels correlated with therapy.

Postmortem examination disclosed the following findings: (1) carcinoma of stomach (surgical removal 10 years previously), with secondary involvement of the lymph nodes, colon, peritoneum, mesentery, ureters, urinary bladder, seminal vesicles, skeleton (generalized), and lungs (fig. 4); (2) bronchopneumonia, confluent and bilateral, due to hemolytic Staphylococcus aureus; and (3) spinal epidural hematoma, with compression of the spinal cord. The prostate gland was semiserially sectioned and failed to disclose any evidence of malignancy, either primary or secondary, despite involvement of the seminal vesicles and periprostatic tissues.

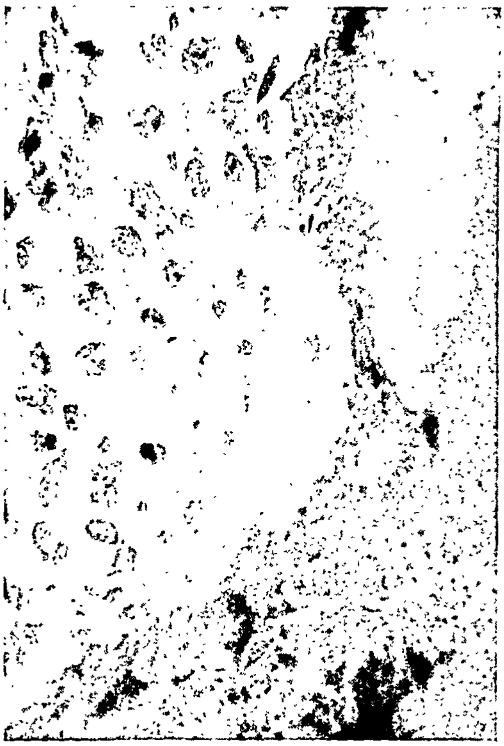

Fig. 4.—Microscopic section of bone marrow, showing sheets of poorly differentiated epithelial cells replacing marrow, similar to those seen previously in stomach and lymph nodes (× 713).

Comment

In spite of our clinical impression, in the present case, of not dealing with a carcinoma of the prostate gland, we finally chose, after a few weeks of careful observation and deliberation with the patient's family, to institute hormonal and surgical therapy as currently accepted for carcinoma of the prostate with secondary spread. To put it plainly, the persistent increase in the total phosphatase level as well as the acid "prostatic" fraction seemed weighty enough, in the light of present knowledge, to warn us not to fail to accept the only possible therapeutic hope that could be offered.

Were we going to treat the patient on the basis of laboratory data only? On the surface it might seem so. We felt, however, that by completely disregarding the findings of the increased "prostatic" enzyme level, we thus also would completely disregard the patient, as no therapeutic avenue of approach seemed otherwise open to him.

A number of reports [11] have indicated elevation of the serum "prostatic" acid phosphatase level in a variety of conditions other than prostatic carcinoma. These include prostatic hyperplasia, infection, massage or trauma of the prostate, testosterone therapy, nonprostatic malignancy, Gaucher's disease, and certain other liver, bone, renal, and miscellaneous disorders. By histochemical techniques for detection of acid phosphatase in tissues [12] acid phosphatase has been observed in both normal and malignant tissue of the spleen, kidney, adrenal, breast, bronchus, marrow, liver, skin, bladder, esophagus, colon, rectum, and stomach. Changus and Dunlap [13] found higher levels of acid phosphatase in the gastric washings of patients with gastric carcinoma than in washings from normal controls. However, prior to the present report, we failed to find a recorded instance of elevation of the serum acid phosphatase level due to disseminated gastric carcinoma.

The clinical usefulness of serum acid phosphatase determinations, even with the refinement of Fishman and Lerner (L-tartrate inhibition),[7] is rather limited. Clinical management of an individual patient will rarely be determined by the acid phosphatase level. The level of serum "prostatic" acid phosphatase can be misleading when elevated, as herein illustrated. Few urologists would subject a patient to confirmatory biopsy until other clinical signs appeared; an abnormal biochemical test result serves principally to raise the index of suspicion and encourage closer observation in succeeding years. A normal level in the presence of prostatic malignancy, particularly localized or early cases, has lessened the diagnostic value of the test and has not supported the earlier enthusiasm of Fishman and associates.[8] A patient in whom early carcinoma is suspected, by the detection of a firm, discrete nodule in the prostate by digital rectal examination, must submit to tissue biopsy, despite a normal acid phosphatase level, in order to confirm or exclude malignancy. In such a patient exhibiting an elevated serum acid phosphatase level it is felt by some that the abnormal level indicates dissemination of the malignancy and that this precludes radical surgery.[11a] However, usefulness of the determination in this particular regard is by no means uniformly accepted.

The possible usefulness of serum prostatic acid phosphatase determinations in following the clinical course of a patient after treatment for prostatic carcinoma was considered by Nobles and co-workers.[11a] They found inconstant correlation between reactivation of malignancy after an endocrine-induced remission and elevation of the "prostatic" serum acid phosphatase level. The test was a poor index of tumor activity. However, they did feel that it might be of value in following the progress of patients after radical prostatectomy, slight elevation above the usual low level possibly indicating recurrence of disease.

Summary and Conclusions

Abnormal elevation of total and "prostatic" serum acid phosphatase levels was associated with widespread dissemination of gastric carcinoma and the absence of prostatic malignancy in a patient previously operated on for the carcinoma. This is the first such case to be reported. The patient survived 10 years after gastric surgery. We are unable to explain the chemical and temporary subjective improvement produced by cortisone therapy.

Serum acid phosphatase determinations, either total or "prostatic," have limited clinical usefulness at present, other than lending support to an already suspected diagnosis of prostatic malignancy. A normal level does not rule out prostatic malignancy, and an elevation is not necessarily diagnostic of it. It is to be hoped and anticipated that further refinements or modifications may one day render this procedure more than an occasionally useful determination.

170 Maple Ave. (Dr. Simon).

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REBIRTH OF GENERAL PRACTICE

Samuel A. Garlan, M.D., New York

I bring you good news: general practice is alive; it is growing; it is wonderfully dynamic. In the not too distant past this field of medicine was the victim of false prophets of doom. In all areas of the world there is clear evidence that the demand has never been greater or the need more urgent for the benefits to mankind that can be provided only by the general practitioner. Never before have there been such opportunities for service.

Three years ago our British colleague John Hunt entitled his Lloyd Roberts lecture "The Renaissance of General Practice." How apt a title; if ever contemporary man had to find the da Vinci or Galileo or even the Erasmus who is now looked on as the essence of what the historians call the Renaissance man (the man who, adept at many things, shone brilliantly in several), then he would in the final analysis turn to the general practitioner.

There is a renaissance in general practice—a world-wide movement concerned with the academic welfare and the scientific encouragement of family doctors on every continent. This movement recognizes that modern medicine, to do its greatest good, must reach patients promptly in and near their homes.

The destiny of general practice as a branch of modern medicine has been the subject of considerable discourse for the past 10 to 15 years. So much of this discourse has resulted in such an unflattering image of the family doctor that one might think we have no reason for being, and have no defense. I submit—we need no defense.

The one unfortunate aspect in this picture is that, while the movement is widespread, it is so only in those parts of the world where the medical profession remains sufficiently free of government domination to permit a continuation of the historical doctor-patient relationship on which the successful practice of medicine must depend.

In 1940 only one of every 10 medical students planned to enter general practice. Medical science has become more complex, and in large communities no family doctor can possibly be truly general. A considerable part of what was once done in a simple way by a family doctor must now be carried out by a team of experts, preferably under the direction of the general practitioner. Currently more than one-half of the medical schools in the United States include family physicians on their staffs. Many hospitals have general practice departments. Since the establishment of the American Academy of General Practice the percentage of medical school graduates entering general practice has risen from 30% (1946) to 51%. The signs of rebirth of general practice are not limited to the United States. The family doctor is once again being recognized as an important element in the science of medicine.

The General Practitioner Today

The general practitioner today is truly the family doctor. The patient as a whole is his main concern. He does not meet only one segment of a patient; he meets a total personality.

Today's family doctor must stand ready to treat most ills of the body and many of the mind and to treat each member of any one family continuously, from the cradle to the grave if necessary. He must have a real understanding of the patient's total

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Chairman's address, read before the Section on General Practice at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1959.

environment. The family doctor offers the family continuing responsibilities for health matters, which include prevention and treatment of any illness or injury affecting the mind or any other part of the body. He realizes the importance of specialties in the total care of the patient and he refers wisely, but he also realizes that without him it would be difficult if not impossible for patient and specialist to meet.

Part of the work of the family doctor today has little visible connection with either illness or injury. He can be called on for premarriage guidance, normal obstetrics, infant feeding, mental health guidance, management of old age, and undertaker negotiations. If the physician is wise enough to protect his own health, continuing care for a family may be from generation to generation. The most important tool available to the general practitioner is his professional skill, but his outlook must be humanistic rather than materialistic. His patient is a human individual rather than a collection of systems. Some years ago an anonymous writer in the British *Lancet* put into rather beautiful prose the quality looked for in every general practitioner:

> Probably the one gift a general practitioner must have or acquire is being able to put himself in the patient's place—see with his eyes the sordid hopeless scene, hear with his ears the cry of the unborn, feel the longing behind the placid face, be in the factory where it happened, sense the closing wall of circumstance, glimpse the colored toy that is the end of all desire, know the slow winding sheet of toxaemia, the hope that flickers in old age and death, and the fear that has no feared thing. In short, sympathy, a subject not in the curriculum.

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There are still parts of this world where the only doctor for hundreds of miles can be only a general practitioner, who cannot limit his doctoring or call in a handy specialist. We can think of Gordon Seagrave in the heart of Burma or Schweitzer in Africa or a United States physician on a submarine or in the wilds of Montana.

Medical science has become more complex, however, and in large communities no family doctor can possibly be truly general. A considerable part of what was once done in a simple way by a family doctor must now be carried out by a team of experts but under the direction of the general practitioner.

The general practitioner of the renaissance is at the center of his community working closely with a host of people. He must work with his general colleagues individually or in a group and with all the specialists and consultants in his area. He works with the other ancillary services absolutely necessary for his own task: secretaries, receptionists, the laboratory service, x-ray technicians, public health officers, dentists, and the special services for particular categories of patients such as the blind, the mentally ill, and the aged.

The activities of many different people must be coordinated and correlated by the general practitioner to assure that his patient's needs are met. If the patient is to be the recipient of team work, then the general practitioner is the quarterback and calls the signals.

Perhaps because the general practitioner is known so well by so many people and perhaps because he can be seen when he is tired and worn out, there are times when his work appears to be mundane. Perhaps because there is an aura of glamour surrounding the specialist many medical students have become convinced that they could not be successful unless they specialized. The medical schools did little to correct these impressions and in many ways encouraged the concept of research and specialization to the detriment of general medicine. In 1940 only 1 of every 10 medical students planned to enter general practice. It was not long before specialists outnumbered family doctors on many hospital staffs. The general practitioner soon discovered that he was not permitted to engage in many medical and surgical procedures for which he was qualified. People began to lose confidence in the generalist. I am afraid they began to regard him as "a bearded old gentleman with a kindly countenance and frayed cuffs."

As late as 1947 he was described at a New York Academy of Medicine meeting as a doctor who could not get (or afford) specialty training. It is sad that in more recent years the dean of a prominent urban university medical school answered a questionnaire with the scrawled notation, "I am unable to answer this since I didn't know that general practitioners still existed." More recently the august *Yale Journal of Biology and Medicine*[1] explained that general practice was dead, having been killed by the new concept of group practice.

American Academy of General Practice

There are now 25,000 general practitioners who belong to the American Academy of General Practice. Not only do they pay annual dues but each one must obtain 150 hours of postgraduate training every three years to remain a member. Since the establishment of the Academy of General Practice in 1947, the percentage of United States medical school graduates entering general practice has risen from 30% of the 1946 graduates to 51% in the last year for which figures are available.

Currently, more than one-half of the medical schools in the United States include family physicians on their teaching staffs. Last year more than 204 hospitals offered 802 general practice residency positions. This year the academy provided financial assistance to 20 young men working toward the completion of general practice residencies.

We see signs that medical schools are planning to expand programs designed to better prepare students for general practice. Last year some 31 schools conducted special programs to give actual experience in clinical practice under supervision. Included in these special programs were preceptorships with general practitioners, general medical clinics, and family care programs.

There are clear indications that the concept of continuous postgraduate education which was pioneered by the Academy of General Practice will become a pattern for the entire profession and may take precedence over the concept of examinations as a mark of competence. At present there is no other medical association requiring an established number of postgraduate study hours for continued membership. The purpose of the postgraduate program is to help members become better family doctors. It is not designed to change a general practitioner into a pseudospecialist or consultant. The charter members of the academy were aware of the necessity for creating strong incentives to encourage attendance at academy functions, and they also recognized that no doctor ever completes his medical education. If he is to keep pace with progress he must keep studying. Of course this involves a loss of time and some sacrifice of income, but it is more important than either.

Postgraduate Services

It is not always simple for practicing physicians to find the time in which to attend formal classes. In some parts of the country, particularly in the Northwest, there are excellent postgraduate correspondence courses available, but other dramatic measures have been taken that help assure stimulating, dynamic instruction and the free-for-all of typical classroom discussions.

During the last four years, for instance, the postgraduate division of the Albany Medical College has been utilizing an entirely new technique for presenting postgraduate medical instruction to practicing physicians. The method utilizes two-way radio, thus making it easy for physicians within a 150-mile radius of the medical college's radio station to participate in conferences conducted by the medical college faculty and also to enter the discussion or ask questions. The doctors meet at their own community hospitals and through their questions control the discussion of the general subject which is being presented. The radio conferences are held 24 weeks a year from November through April.

Programs and mimeographed teaching aids are distributed in advance of each conference, and the subject and participating faculty are indicated. Seven or eight hospitals are included each day, with the conferences generally being held from 12 noon to 1 p. m. In a number of the hospitals the physician is able to obtain his lunch and participate simultaneously in the conference. There are, of course, times when a doctor cannot get to the hospital, and in that event he may listen in his own office or home and telephone questions to the hospital for transmission to the faculty.

Other devices and methods are used in other parts of the country. In Illinois, the Illinois academy has teams traveling throughout the state conducting one-day and two-day sessions in various but centralized locations. The faculty for these teaching teams is drawn from the major medical schools. In the state of Kansas somewhat similar teams visit towns and hamlets providing courses for family doctors.

Need for Low-Cost Medical Care

General practitioners, because of their intimate relationship with patients and their knowledge of patients' finances are extremely sensitive to the need for low-cost medical care. One of the obvious dangers to medicine today is that of governmental control and regulations. If this comes, it will be because we have invited it to come by not providing health care that the majority of people can afford.

In an attempt to practice good medicine at a price most people can afford, the Group Health Insurance Plan in 1955 launched the Family Doctor Plan, the first free-choice plan to provide "service" (paid-in-full) benefits for almost unlimited home and office care. This, of course, is in addition to the in-hospital services covered by another Group Health Insurance Plan. Preventive services under the Family Doctor Plan include annual physical examinations, well-baby care, and immunizations. The plan is built around the services of the general practitioner and aims to strengthen the patient's relationship with his family doctor by removing the financial barrier that too often comes between them. More than 5,000 general practitioners in the metropolitan New York area are now participating in the plan, and there are some 250,000 subscribers.

New Role of the General Practitioner

Many United States hospitals have general practice departments. These are generally established as administrative departments, and a physician from this department sits on the medical board. Practitioners in these departments are rated by the medical board, and thus we find general practitioners being tested by their peers. This is one answer to those hospitals who claim that their constitutions do not permit general practitioners to sit on the board.

The Academy of General Practice, recognizing the growing interest in the establishment of general practice departments, has published a book containing suggestions and guideposts for the use of hospitals and hospital boards.

Today almost every large state in the United States has a general practice section in its medical organization, and each has a delegate at large who sits in the state House of Delegates. Thus we environment. The family doctor offers the family continuing responsibilities for health matters, which include prevention and treatment of any illness or injury affecting the mind or any other part of the body. He realizes the importance of specialties in the total care of the patient and he refers wisely, but he also realizes that without him it would be difficult if not impossible for patient and specialist to meet.

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American Academy of General Practice

There are now 25,000 general practitioners who belong to the American Academy of General Practice. Not only do they pay annual dues but each one must obtain 150 hours of postgraduate training every three years to remain a member. Since the establishment of the Academy of General Practice in 1947, the percentage of United States medical school graduates entering general practice has risen from 30% of the 1946 graduates to 51% in the last year for which figures are available.

Currently, more than one-half of the medical schools in the United States include family physicians on their teaching staffs. Last year more than 204 hospitals offered 802 general practice residency positions. This year the academy provided financial assistance to 20 young men working toward the completion of general practice residencies.

We see signs that medical schools are planning to expand programs designed to better prepare students for general practice. Last year some 31 schools conducted special programs to give actual

STERCORACEOUS ULCERS OF THE COLON

RELATIVELY NEGLECTED MEDICAL AND SURGICAL PROBLEM

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Stercoraceous ulcers are lesions in the mucous membrane of the colon and rectum caused by pressure of inspissated or impacted fecal masses. This complication of constipation and malnutrition is limited to elderly or bed-confined patients. Penetration of the intestinal wall can occur, with subsequent peritonitis. Stercoraceous ulcers were diligently searched for during 175 nonselected autopsy examinations, because the condition has been so infrequently diagnosed either prior to or after autopsy. This search disclosed that such ulcers had occurred in 10 patients. Perforation with secondary peritonitis was the cause of death in four. Constipation had been a difficulty in six of the patients, and two others had had rectal bleeding. Gross microscopic morbid anatomy of the ulcer is characteristic enough to allow diagnosis, even though the fecal mass may not be found at autopsy.

Ulcerations of the mucosa of the colon and rectum secondary to pressure effects of inspissated or impacted fecal content have long been recognized. The term stercoraceous (or stercoral) ulcer has been most commonly applied to this lesion, which under certain circumstances may progress to perforation of the intestinal wall. Relatively little attention has been given in the literature to this pathological entity of importance to both the surgeon and the internist. Data on 10 cases of stercoraceous ulceration of the large intestine have been collected from our files and form the basis of this study. Four of these cases terminated in perforation of the intestinal wall with the production of a fecal peritonitis. In the others the findings were incidental at the time of autopsy. In none of our cases was there an association with intrinsic or extrinsic obstructive lesions of the intestinal wall. The clinicopathological features as well as the pathological anatomy of patients in our series are presented.

Review of the Literature

There is a striking paucity of literature pertinent to the problem of stercoraceous ulceration. Only a few reports[1] have been found in which perforations secondary to stercoraceous ulceration unassociated with obstructive lesions are clearly indicated. Brief discussions are given in some textbooks of general and surgical pathology with emphasis on the role of obstruction. MacCallum,[2] for example, in his discussion of stenosis and stricture of the intestinal tract, stated that "above the stricture the mucosa of the distended intestine often presents extensive ulcerations which are thought to be due partly to its disturbed nutrition, partly to the stagnation of masses of infected fecal material in contact with it (stercoraceous ulceration)." A similar presentation is offered by Boyd [3] who says that "so-called stercoral ulcers of the mucous membrance develop in the segment above the obstruction, owing to the irritation of the hard scybalous masses that collect there." Although an illustrative gross photograph accompanies his brief discussion, it is of interest that no references are given and his observations appear to be firsthand in nature.

A view not limited to the association with obstructive lesions of the intestine is that of Robbins,[4] who states that "impacted inspissated feces may produce trauma to the intestinal mucosa with the production of so-called 'stercoral ulcers.' These are most common in elderly patients in the terminal rectum where the pressure of surrounding structures does not permit adequate distention." No references are given. Standard textbooks on surgery either make no mention of stercoraceous ulceration [5] or give classifications indicating the presence of such lesions without employing a specific diagnostic term as in Homan's [6] "Textbook of Surgery" where it is stated that "proctitis or inflammation of the rectal mucous membrane, as well as its underlying wall, may be simple or ulcerative. Simple forms are . . . mechanical, the result of the irritation of foreign bodies or hard feces . . . ." A quite similar treatment without elaboration is given by Sigemund.[7]

Sporadic cases of unusual forms or locations of stercoraceous ulceration have been reported by Blotner,[1c] who presented a case of localized necrosis of the cecum produced by a fecalith trapped in a cecal haustration, and by Pollack,[8] who presented a case in which there was involvement of the terminal ileum secondary to a carcinoid of the ileum.

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that general practice is closely integrated in the organizational sections of the state medical societies as well as in the A. M. A.

The signs of rebirth in general practice are not limited to the United States. In 1952 the College of General Practice was founded in England. Although coming shortly after the founding of the academy here, the founding of the English college was entirely independent of the American academy and was the result of an entirely spontaneous movement among groups of general practitioners there.

Within three weeks of its founding it had 1,200 members, and the membership is now well over 6,000. The college has developed 35 regional faculties, 13 of them overseas in Eire, Australia, New Zealand, Africa, and other areas.

Five years ago the Canadian College of General Practice was founded, primarily as an educational body concerned with the continuing postgraduate education of general practitioners. Its basic objective is to keep the general physician abreast of modern medicine, and all activities are directly to benefit all general physicians whether they are members of the college or not. More than a fifth of Canada's family doctors are members. Membership there is dependent on the acquisition of 100 hours of postgraduate credit every two years.

The largest group in the Pan American Medical Association is the Section of General Practice, and this section will have the major part of the Pan American Congress in the spring of 1960.

A large percentage of the doctors in Latin America are general practitioners, regardless of their previous training or personal inclinations. In an area where there are 2 physicians for every 10,000 people (compared to 13.5 per 10,000 in the United States), a man has very little choice but to practice general medicine. The medical director of a large oil company in the area told me that in its early years in the South American countries the company would send various specialists to work with drilling and pipeline crews. In very short order these men were practicing every type of medicine possible, and their patients were traveling hundreds of miles to see them. Now that company employs mainly general practitioners so that they will be qualified to handle whatever medical condition arises.

I observed on a recent visit to North Africa that in the city of Tangiers essentially all physicians are general practitioners. There is a shortage of doctors, and a man is required to practice general medicine if he is going to serve that city.

On Dec. 29, 1955, for the first time in the history of the Netherlands community of physicians, a group of general practitioners from all parts of that country met in order to exchange views on the practice of their specific science. On that day it was decided to establish the Netherlands Association of General Practice. The Netherlands association is concerned with the training and postgraduate education of the family doctor. Within months of its founding over 14% of the general practitioners in the Netherlands were enrolled.

The publications of the American Academy of General Practice and the various colleges of general practice are among the best to be found. The American academy's *GP,* an outstanding medical publication, is designed for the family doctor. The *Research Newsletter* of the English College is an invaluable aid to all family doctors.

The family doctor is once again being recognized as the most important element in the science of medicine. There are temporary handicaps, particularly in the larger cities where family doctors may find it exceedingly difficult to practice in the larger hospitals. People want and need more than a cool appraisal of a segment of their bodies; they want a friend and confidant. Patients are not inanimate objects passing before our eyes on some sort of assembly line; they have fears and desires, likes and dislikes, even as you and I. Despite the universal rebirth of the family doctor, there is a grave challenge before us.

Need for the General Practitioner

American and European medical schools have a serious responsibility to encourage and train general practitioners. The specialists are, by and large, located in the countries with the highest standards of living and then usually only in the most populated cities. Many areas in this world—yes, even in the United States—are in need of doctors—now. They need doctors who can serve families easily and economically.

Some weeks ago Dr. Milton Eisenhower stated that the most effective means of proving to the world that democracy is a dynamic force is by generating a movement to improve the health of people in underdeveloped sections of the world. If our medical schools continue to emphasize medical research and specialization to the detriment of general medicine, how do we fill the desperate world-wide need for basic medical care?

Our rebirth must continue; it must be nurtured with care, efficiency, and strong scholastic support. Our only desire is to minister to those who need us. Whatever future form medicine takes in its efforts to serve the public, be it in group practice, clinics, or health plans, the general practitioner will remain as the quarterback of the team. He is the man equipped to minister to 85% of human ailments; he is the man who will continue to have direct contact with a patient's home and family; and he is the man who is in the position to coordinate the many services now working for the well-being of human beings.

101 Central Park, West (23).

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stercoraceous ulcerations, giving an over-all incidence of 4.6%. The average age was 68.6 years with a range from 42 to 83 years. There were 6 males and 4 females in the total group of 10 patients. In six cases constipation was recorded in the clinical records. In three cases constipation had not been recorded, but diarrhea associated with bright red rectal bleeding was present in two of these. In only one case was neither constipation nor diarrhea recorded; however, the patient was admitted in shock and died in four hours without an adequately taken history. Of the total of six cases in which constipation was recorded, it is of interest that in two there were also episodes of rectal bleeding. Of the total 10 patients studied, 6 developed complications. In four (cases 1 through 4) there was progression to either single or multiple perforations at the site of ulceration with fecal peritonitis. Two (cases 5 and 6) developed marked rectal hemorrhage which dominated the clinical picture and overshadowed the initial admission complaints (see table).

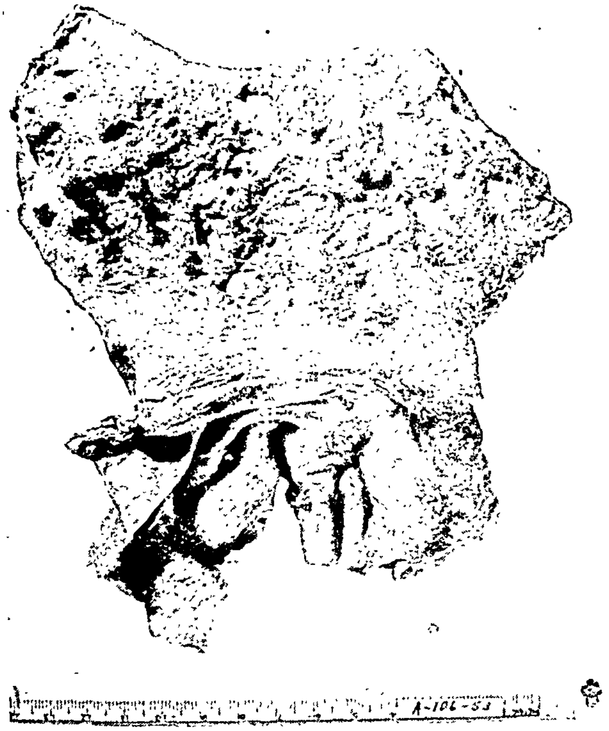


Fig. 1.—Numerous sharply marginated superficial or deep ulcerations of terminal rectum separated by intact rectal mucosa. Varied shapes of ulcers coincide with surface contour of impacted fecal masses.

Gross Observations.—In 8 of 10 patients the ulcerations were limited to the area of the rectosigmoid (fig. 1 and 2). Three of these patients had single ulcers. Five had two or more ulcers, often closely approximated. In the two remaining patients, multiple ulcers had a more widespread distribution. In one they were localized to the ascending colon with perforations in both the cecum and the transverse colon. In the other, multiple ulcers were found in the cecum, transverse colon, and rectosigmoid. The ulcers ranged in size from 2.5 to 10.7 cm. in greatest diameter. They were characterized by irregular geographical outlines which conformed to the surface contours of fecal masses when present. There was sharp demarcation between the margins of ulceration and the adjacent mucosa. The surfaces of the ulcerated zones generally had some degree of dark purplish discoloration frequently with patches that were greenish-gray or yellowish-gray.

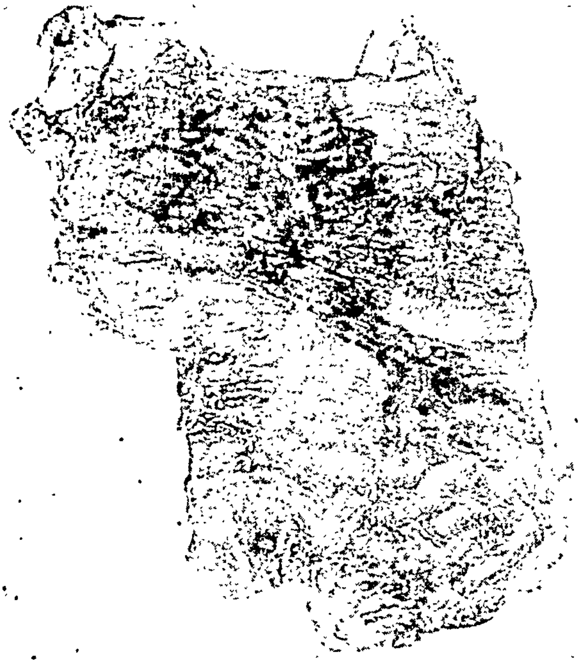


Fig. 2.—Large circumferential irregular ulcer of rectosigmoid showing exposed transverse bundles of the muscularis.

A consistent finding was the depression of the ulcerated surface below the mucosal base line with varying degrees of stretching and thinning of the involved intestinal segment. Perforation occurred generally in the central portions of the ulcerations where thinning of the wall was maximum. When ulceration was extensive, it was not uncommon to be able to identify the fibers of the underlying exposed muscularis. In the earliest stages of stercoraceous ulceration, an "ironed-out" appearance of the mucosa with various degrees of pallor was conspicuous. However, with the advent of excoriation various degrees of purplish discoloration appeared. The major blood vessels, even in the presence of extensive ulceration, failed to show significant sclerosis or thromboses.

Microscopic Observations.—Sections through the zones of ulceration revealed that the mucosal aspect of the intestinal wall was denuded with loss of

Material and Methods

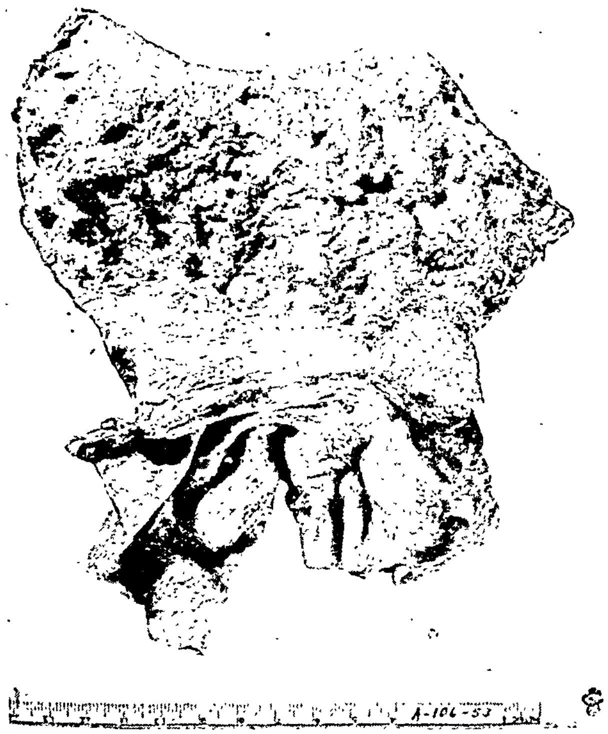
In routine autopsy studies over a period of 12 months, care was exercised to make a critical evaluation of the rectum and rectal ampulla. In this period eight cases of stercoraceous ulceration were observed, five of which were found to be directly associated with hard fecal masses in the regions of ulceration. In the three remaining cases there were ulcerations not associated with the presence of hard fecal masses but which had gross characteristics indistinguishable from those of the first group. The blood supply to the rectosigmoid and rectal ampulla was studied in each case in order to determine if vascular disease was present which could account for or contribute to these ulcerations. Examination of the autopsy protocols of Mount Sinai Hospital for a period of four years prior to this study revealed an additional two cases which had been recorded only because of their dramatic clinical manifestations. Sections from the ulcerated zones and adjacent intestinal wall were studied initially with the usual hematoxylin-eosin preparations, and special stains for micro-organisms were utilized as indicated.

Data on Ten Cases of Stercoraceous Ulcers of the Large Intestine

Case No.	Sex	Age, Yr.	Principal Pathological Diagnoses	Clinical Data	Gross Findings	Comment
1	F	74	Stercoraceous ulcers of the rectosigmoid, with perforation and purulent peritonitis; arteriosclerotic heart disease and diabetic glomerulosclerosis	Admitted in shock; died 4 hr later; vomiting 4 days before admission; bedridden 2 yr.	Hard fecal impactions in rectosigmoid; paper-thin wall with multiple punched-out closely spaced ulcers; small perforations in several ulcers; fecal material and pus in peritoneal cavity	Diabetes mellitus, 7 yr.
2	M	76	Stercoraceous ulcers of the transverse colon, with perforation and purulent peritonitis; arteriosclerotic heart disease; early Laennec's cirrhosis	Admitted with urinary retention; prostatectomy followed by obstruction of small intestine; lysis of adhesions; wound dehiscence 5th postoperative day; persistent distention with poor healing	Fecal impaction from cecum to transverse colon; small ulcers in cecum, 2 with pinpoint perforations; ulcers of transverse colon with a 1-cm. perforation in midportion; pus and fecal material in peritoneal cavity	Constipation throughout hospital stay; no response to therapy
3	M	66	Stercoraceous ulcer of the rectosigmoid, with perforation and purulent peritonitis; arteriosclerotic heart disease; metastatic carcinoma of brain, primary undetermined	Admitted in coma of 2 days' duration; history of paresis on right; progressive deterioration; died 30th hospital day	7-cm. geographical ulceration of rectosigmoid 16 cm. from anus; margins of ulcer conformed to contour of large hard fecal mass; 0.5-cm. perforation with purulent exudate on serosa	No stools recorded in hospital chart for 5 days
4	F	69	Stercoraceous ulcers of the rectosigmoid, with perforation and purulent peritonitis; multiple stercoraceous ulcers of rectum	Admitted for vomiting; fecal impaction found; coma and shock developed with abdominal rigidity and distention; death 14 hr. after admission	3 geographical ulcerations in rectosigmoids; largest 7 cm. in diameter with 3-cm. perforation in central portion; lowermost ulceration in rectal ampulla; outline of all conformed to contour of fecal masses; pus and fecal material in peritoneal cavity	Diabetes mellitus of several years duration
5	M	72	Stercoraceous ulcers of rectosigmoid; healed posteroseptal myocardial infarction; lobar pneumonia on right	Admitted in severe congestive failure; stool incontinence and dark red rectal bleeding on 16th hospital day; recurrence on 22nd and 23rd days with large red clots per rectum	2 geographical ulcers in mi[illegible]gmoid; largest 11 cm. in diameter; 3rd ulcer in rectal ampulla; no local vascular abnormality	Rectosigmoid ulcerations only lesions to account for dark red bleeding per rectum; no esophageal varices
6	M	65	Stercoraceous ulcers of rectosigmoid; pulmonary emboli with infarcts; mural thrombus; right auricular appendage	Admitted for electroshock therapy for depression; several episodes of fecal impaction prior to treatment; pulmonary infarcts during treatment; anticoagulants given; markedly prolonged prothrombin time	2 geographical ulcers in rectum adjacent to ampulla; largest 6 cm. in diameter; 250-cc of gelatinous blood clot and softened fecal material in rectosigmoid	Presence of stercoraceous ulcer with irritation of amp[illegible] probably accounts for episodes of fecal incontinence
7	F	42	Stercoraceous ulcer of rectum; rheumatic heart disease with mitral stenosis; cerebral infarcts	Previous admissions for rheumatic heart disease and congestive failure; final admission for cerebrovascular accident with paresis; died 7th hospital day	5-cm. geographical ulcer in rectal ampulla adjacent to anorectal junction; outline conformed to contour of hard fecal mass	Record of only one stool in 7 days
8	M	83	Stercoraceous ulcer of rectum; gangrenous cholecystitis with peritonitis; penetrating gastric ulcer	Admitted for bloody diarrhea of 2 weeks' duration; semicomatose and dehydrated; signs of acute abdomen on 9th day; died 13th day	6.5 cm. geographical ulcer in rectum; base covered with yellowish green, dry membrane; major blood vessels in area free of thrombi or significant sclerosis, grossly	Fecal incontinence during hospitalization accompanied by passage of dark red blood clots and bright red blood
9	M	76	Stercoraceous ulcers of rectum; bronchiectasis and bronchopneumonia; cor pulmonale	Known cardiac disease; admitted in congestive failure; refractory to treatment; died on 17th hospital day	Marked hyperemia of rectal mucosa; 2 geographical ulcerations up to 2.5 cm. in diameter, confined to rectum	Initially constipated for 15 days; only 2 spontaneous stools recorded during hospitalization; developed terminal fecal incontinence
10	F	62	Stercoraceous ulcers of colon and rectum; arteriosclerotic heart disease with old infarct; diabetic glomerulosclerosis	Diabetes and congestive failure; admitted with vomiting and blurring of vision; developed diarrhea; progressive deterioration with terminal azotemia	3 large geographical ulcers present; one each in cecum, transverse colon, and greater part of rectum; mucosa of remaining colon not altered	Diabetes mellitus

Clinical Data

In the period from June, 1956, through June, 1957, 175 autopsies were performed on adults. Of these, eight showed the presence of one or more stercoraceous ulcerations, giving an over-all incidence of 4.6%. The average age was 68.6 years with a range from 42 to 83 years. There were 6 males and 4 females in the total group of 10 patients. In six cases constipation was recorded in the clinical records. In three cases constipation had not been recorded, but diarrhea associated with bright red rectal bleeding was present in two of these. In only one case was neither constipation nor diarrhea recorded; however, the patient was admitted in shock and died in four hours without an adequately taken history. Of the total of six cases in which constipation was recorded, it is of interest that in two there were also episodes of rectal bleeding. Of the total 10 patients studied, 6 developed complications. In four (cases 1 through 4) there was progression to either single or multiple perforations at the site of ulceration with fecal peritonitis. Two (cases 5 and 6) developed marked rectal hemorrhage which dominated the clinical picture and overshadowed the initial admission complaints (see table).



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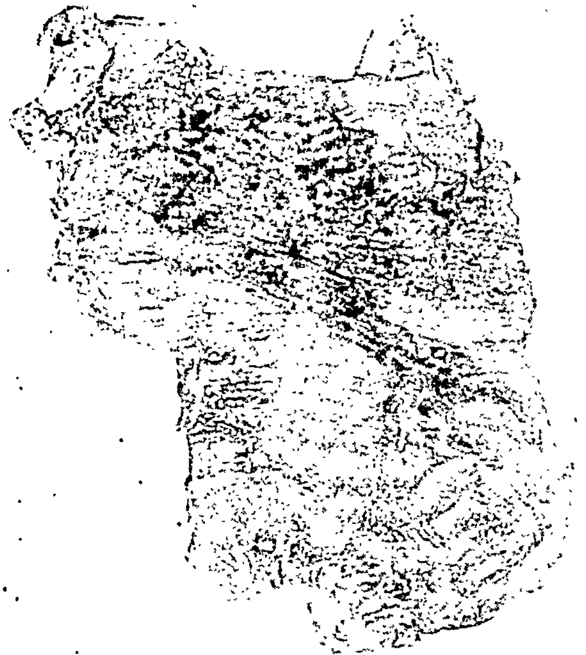

Fig. 2.—Large circumferential irregular ulcer of rectosigmoid showing exposed transverse bundles of the muscularis.

A consistent finding was the depression of the ulcerated surface below the mucosal base line with varying degrees of stretching and thinning of the involved intestinal segment. Perforation occurred generally in the central portions of the ulcerations where thinning of the wall was maximum. When ulceration was extensive, it was not uncommon to be able to identify the fibers of the underlying exposed muscularis. In the earliest stages of stercoraceous ulceration, an "ironed-out" appearance of the mucosa with various degrees of pallor was conspicuous. However, with the advent of excoriation various degrees of purplish discoloration appeared. The major blood vessels, even in the presence of extensive ulceration, failed to show significant sclerosis or thromboses.

Microscopic Observations.—Sections through the zones of ulceration revealed that the mucosal aspect of the intestinal wall was denuded with loss of substance to varying depths (fig. 3, 4, 5, and 6). The surface was generally characterized by a lamella of ischemic necrosis revealing a loss of staining affinity but also presenting a paucity of inflammatory elements. In some foci fragments of inspissated granular basophilic fecal material abutted on the surface. Numerous plump bacteria of the bacillary or coccoid type were present among the necrotic surface tissues, giving the surface lamella a pale bluish cast in some regions of the hematoxylin and eosin preparations. No large or clustered colonies were seen however. The tissues immediately adjacent exhibited pressure condensation, and vascular channels were either compressed or distended and contained bland thrombi.

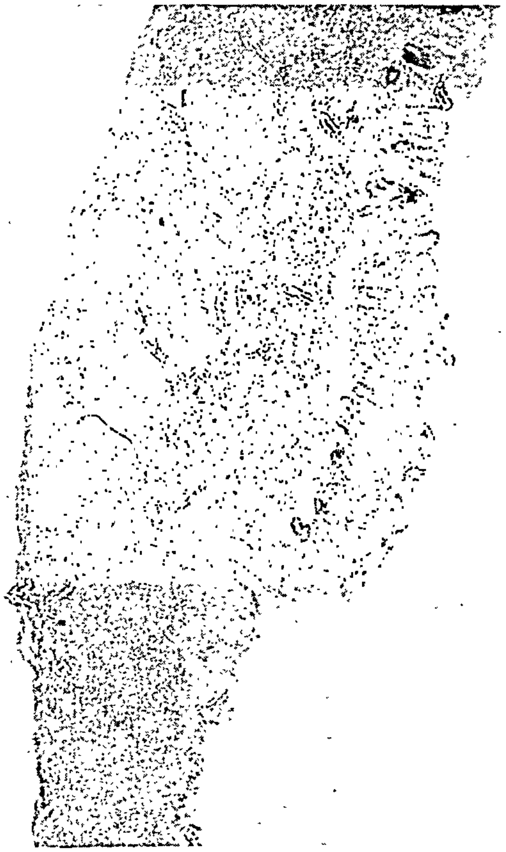

Fig. 3.—Sharp junction between rectal musoca and ulcerated zone. Ulcer base and adjacent wall of rectum show negligible cellular reaction. Hematoxylin-eosin stain (× 20).

A mild inflammatory reaction was present, consisting principally of macrophages with a sprinkling of polymorphonuclear leukocytes. In zones where necrosis had extended to the tunica adventitia, an intense inflammatory reaction and frank focal fat necrosis or suppuration had occurred. It was not uncommon to find small masses of deeply basophilic granular fecal material, including vegetable fibers, in scattered zones when the penetration of the intestinal wall had reached this depth. The character of the cellular response was variable but consisted predominantly of macrophages with conspicuous lipophagic transformation. Lymphocytes were seen focally in appreciable numbers. Small vessels containing bland thrombi were not uncommon in the adventitial fat. When perforation was present, frankly suppurative peritonitis developed.

When the rectal wall had been exposed to a lesser pressure effect, the mucosa was only superficially denuded and the lamina propria mucosae and submucosa had been considerably compressed. It was not uncommon to see glandular elements abutting on the muscularis. The inflammatory reaction was more striking and extended into the muscularis but remained basically of a subacute nature, with not more than 25% polymorphonuclear leukocytes. The remaining elements were plasma cells, eosinophils, lymphocytes, and macrophages. Bacterial invasion of the mucosa and subjacent issue was not seen, and a surface zone of necrosis was absent.

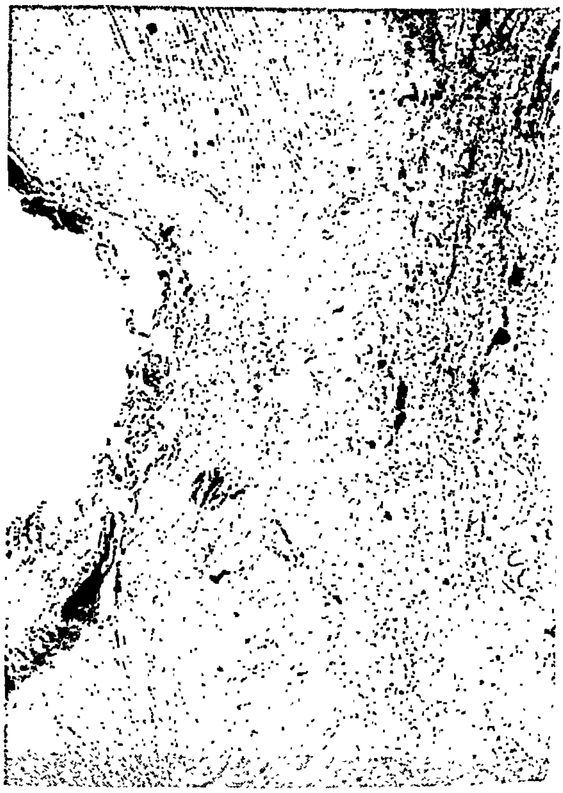

Fig. 4.—Penetrating ulcer of rectum showing necrotic surface lamella and scant inflammatory response except in perirectal fat. Hematoxylin-eosin stain (× 25).

Comment

It is evident from the material presented that we have made the diagnosis of stercoraceous ulceration at autopsy even in the absence of inspissated hard fecal masses distending the intestinal lumen. In five cases the ulcerations conformed to the contour of hard fecal masses distending the involved intestinal segment. This included the four cases in which perforation had occurred. In three additional cases hard impacted stool was not present, but the ulcers in both gross and microscopic characteristics were indistinguishable from those in which hard impacted fecal material had been present. In these three instances the clinical course was one of constipation followed by a terminal episode of bloody diarrhea. We believe this was instrumental in softening and passing the impacted stool. In one of the remaining cases (number 9) constipation was a dominant feature requiring repeated enemas. In this case there was development of terminal fecal incontinence. The two ulcers found in this case were restricted to the rectum and were indistinguishable from the group as a whole. In the last case (number 10), although no mention of constipation was present in the clinical records, the patient had been hospitalized for congestive heart failure and had the onset of profuse diarrhea six days after admission. The ulcerations of the cecum, tranverse colon, and rectum were in every way typical of the group.

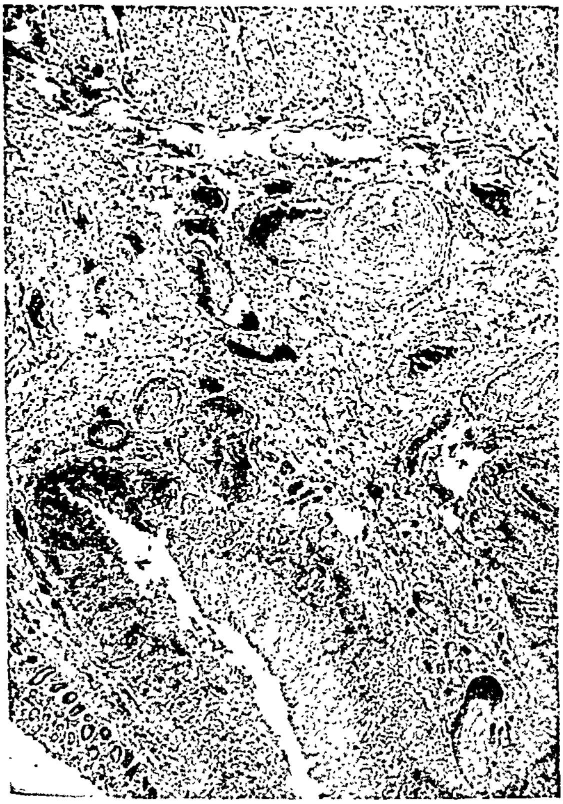

Fig. 5.—Bland fibrin thrombi and scant cellular reaction in submucosa of rectum bordering stercoraceous ulcer. Hematoxylin-eosin stain (× 40).

A review of the literature reveals only a few reports concerning the effects of impacted fecal material on the colon. These were reported principally because of massive fecal impaction or, as in the case reported by O'Reilly,[9] because of secondary perforation. Various reports[10] have emphasized the association of large intestinal perforations with primary obstructive lesions or diverticulitis. No reports have been found giving an indication as to what may be the actual frequency of stercoraceous ulcers found at autopsy. There may be several possible reasons for the failure to recognize stercoraceous ulcers at their true incidence. It is not an uncommon practice to cut the terminal region of the colon at a relatively high level, leaving a substantial segment of the rectosigmoid in the body unexamined. A further common practice is to delegate the opening and, on occasion, even the inspection of the intestine to a morgue attendant or untrained observer. Andrews[1a] states that "impactions of the rectum and colon occur more frequently than the literature suggests. Their diagnosis and treatment are usually passed over lightly. The complications and morbidity associated seldom are diagnosed as such and are even more rarely reported."

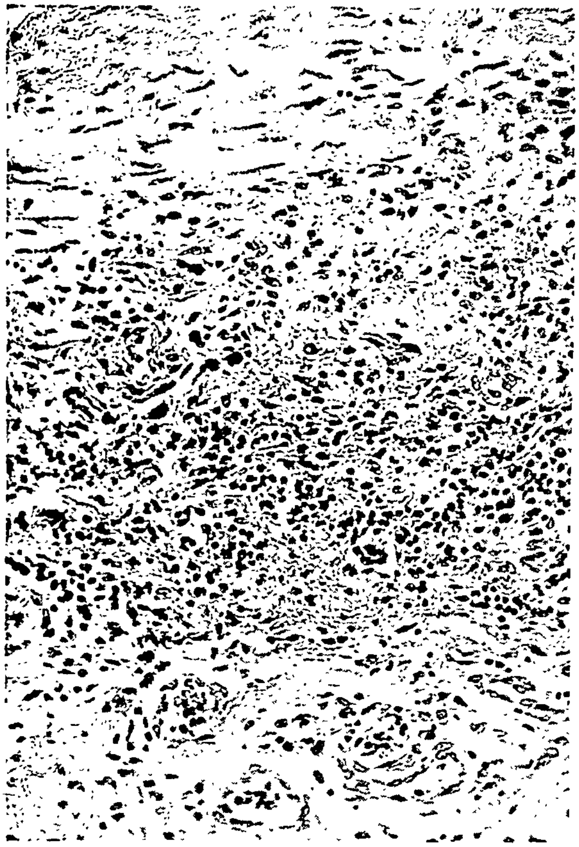

Fig. 6.—Moderate mononuclear cell reaction seen in submucosa beneath base of some stercoraceous ulcers. Hematoxylin-eosin stain (× 215).

It appears that stercoraceous ulceration does not commonly occur in the presence of normal bowel function. In all but one of our cases abnormal bowel function was manifested clinically, and in the remaining case the patient was admitted in terminal shock without an adequately taken history. All cases occurred in association with illnesses in which bowel dysfunction, principally constipation, not uncommonly presents a clinical problem, e. g., congestive heart failure or cerebrovascular accidents. Apparently paradoxical signs and symptoms such as diarrhea and a continuous desire to defecate, which may be misinterpreted as diarrhea, may occur in association with fecal impaction.

This has been recognized by Andrews[1a] who *states that* "*with rectal impactions there may* be frequent stools and a continuous desire to defecate. This often is interpreted as diarrhea and the true condition not suspected. The occurrence of bright red rectal bleeding and the passage of blood clots should arouse some suspicions as to the possible presence of stercoral ulceration(*s*)." In our case 5 there was rectal bleeding which was diagnosed and treated as esophageal varices. Case 6 presents a special problem in that anticoagulant therapy had been administered because of multiple pulmonary infarcts. At one time this patient's clotting activity had been less than 10% of normal. This certainly would not constitute a contraindication to the use of anticoagulant therapy but should alert the clinician to a possible source of rectal bleeding in patients under such therapy.

Summary

Ten cases of stercoraceous ulceration were seen at autopsy. None was associated with either intrinsic or extrinsic obstructive intestinal wall lesions. The cases fall into three main categories: four with rupture and peritonitis, two associated with rectal hemorrhage, and four as incidental findings at autopsy, with signs and symptoms of abnormal bowel function. There are distinctive gross and microscopic characteristics of the lesion.

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PSYCHOLOGY AND AUDIOLOGY IN GERIATRIC REHABILITATION.—Certain problems of estimating dysfunction in the geriatric patient are common to clinical audiology and psychology in that both disciplines must deal with sensation, perception, and cognition in relation to language and communication. Both audiologist and psychologist are concerned with (1) problems of testing, (2) relating test results to life situations, and (3) personality influences on test results. . . . By means of special and standardized tests, he [the patient] is presented with a variety of selected stimuli designed to elicit information on the sensory input in regard to sensation and comprehension and perception and cognition. Test items are presented, and, from his responses, inferences are made as to what is and what is not a sensory experience for him. These procedures have proved to be adequate for evaluating the average younger person. However, for many geriatric patients, they have not led to reliable or valid results. This should not be surprising, since the tests have not been standardized for these patients. How can the clinical audiologist and psychologist improve testing techniques for the geriatric patient? . . .

Personality factors . . . influence test results. The psychologist is expected to relate the personality trends of the geriatric patient to the treatment. . . . The audiologist is also confronted with personality characteristics which have a direct bearing on test results. In addition to reporting the audiologic results of the hearing examination, the audiologist should not hesitate to include a statement on the behavioral characteristics of the patient and how they affected the test results. For example, it would be useful to know that a particular patient is an impulsive individual who is quick to respond at the slightest hint that he has "heard" the stimulus.—I. Belmont, Ph.D., Common Problems of Clinical Psychology and Audiology in Geriatric Rehabilitation, *Geriatrics*, August, 1959.

PSYCHOPHYSIOLOGICAL APPROACH TO MANAGEMENT OF PATIENTS WITH CONGESTIVE HEART FAILURE

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To facilitate an appreciation of the psychosomatic implications of congestive heart failure, the emotional problems of 30 patients being treated for cardiac decompensation were defined. Emotional difficulties of a chronic nature were found to be an integral part of daily living in 26. Cardiac decompensation because the patient fails to take digitalis which failure, in turn, is the result of his emotional problem is an example of indirect relationship between the mental and organic maladies. This was present in 14 patients. In 19 an acute emotional stress such as the death of a beloved relative had a more direct influence, through as yet only partially understood neurohumoral mechanisms, in prolonging or precipitating an episode of congestive failure. The practical implication of these psychosomatic relationships is indicated by the known facts that heart function, venous pressure, and arterial pressure are all affected by emotional stress or by hormones released at the time of stress.

The syndrome of congestive heart failure is a disturbance not only of the cardiovascular system but of the total organism, and the clinical picture is often a consequence of altered function in various systems, e. g., pulmonary, hepatic, or renal. In addition, there is evidence that the central nervous system, particularly the hypothalamus and the pituitary-adrenal complex, is involved in the development and perpetuation of congestive heart failure.[1]

Whatever the precise sequence of pathological events, the fundamental derangement in congestive heart failure is the inability of the heart to do the work required of it. Failure occurs when cumulative forces overcome the cardiovascular regulatory mechanisms and deplete the cardiac reserve. Therapy is focused on improvement of cardiac function by increasing the cardiovascular reserve and reducing the work demands on the heart.

The present discussion is concerned primarily with psychological and interpersonal factors which appear to affect or be affected by congestive heart failure or play a role in the sequence of events leading to its development, exacerbation, or perpetuation. The application of this view to the clinical situation may be important.

Review of the Literature

Textbooks recommend cultivation of "peace of mind" and "mental repose" in the management of the patient with congestive heart failure. Until recently there were few physiological or psychological data, of other than impressionistic nature, to support such recommendations. A substantial body of data has accumulated in recent years regarding the psychophysiology of the circulation, and psychological changes or emotional reactions have been correlated with cardiovascular changes, as measured by pulse rate, rhythm, stroke volume, cardiac output, peripheral resistance, and arterial pressure.[2] It has been observed that subjects with both normal and abnormal hearts recover from exercise less efficiently during states of emotional tension.[3] In addition, recent studies indicate that emotional factors may affect both peripheral and central venous pressures.[4]

Humoral mechanisms in cardiovascular function and in emotional states have also been studied. Epinephrine and arterenol are accepted as important endogenous chemical substances which are physiologically involved in emotional responses. Their effects on venous circulation are described by Eckstein and Hamilton [5] and Guyton and coworkers [6] and are pertinent to the over-all understanding of cardiovascular decompensation. Aldosterone, which has been shown to increase in states of anxiety,[7] has been studied in relation to its role in the development of edema in heart failure.[1] Antidiuretic activity is also increased by emotional or noxious stimuli [8] and may play a role in the clinical picture, especially late in the disease process.[1]

The studies mentioned above suggest some of the mechanisms by which emotional states, through neurohumoral pathways, may influence cardiovascular function. A consideration of these influences on the patient with congestive heart failure, therefore, may be of practical significance in the management of this condition.

Clinical studies of the relative significance of various precipitating factors in congestive heart failure are limited. Sodeman and Burch [9] examined 100 consecutive patients from whom they obtained de-

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tailed information about 104 episodes of congestive failure. In 55 of these episodes precipitating factors could be identified, and in 40 of the 55 compensation was effected rapidly. In 47 patients no precipitating factors were demonstrated, and 46 of these were considered to have a poor prognosis because decompensation persisted. "Psychic trauma" was considered to have been the precipitating factor in two patients. Boyer and co-workers[10] studied a series of 1,000 case histories. In 561 of these such precipitating factors as myocardial infarction, hyperthyroidism, and physical exertion were identified. In 439 patients no precipitating factors were reported. "Emotions" were thought to have precipitated failure in only one patient. In about half of the patients in both of these series there were no apparent explanations for the occurrence of congestive failure at the particular time it appeared. Many patients had an unexplained, insidious onset of congestive heart failure. In both series apparently no explicit search was made for possible emotional factors influencing the onset or course of heart failure. Prevention of illness requires an answer to the question, "Why does the patient become ill at this particular time?"

Synopses of Thirty Cases of Congestive Heart Failure (CHF)

		Emotional Influences		
Case No.	Patient Data*	Acute Indirect	Acute Direct	Chronic
1	58, C, M, hypertensive and arteriosclerotic heart disease and obesity, class 3	Dependency of illness unacceptable → (blow to self esteem) denial of illness → inadequate diet, rest, and medication → perpetuation of CHF	Probable: (a) loss of brother → exacerbation; (b) loss of cousin with heart disease → exacerbation of CHF	Daughter's chronic illness, wife's poor health
2	50, C, M, arteriosclerotic heart disease, class 3	Loss of ability to work → felt helpless and restless → denial of illness → continued work → perpetuation of CHF	Undetermined	Financial crisis, daughter's marital trouble, wife's poor health
3	27, C, M, congenital heart disease (interventricular septal defect), class 1	Undetermined	Probable: illness and death of aunt with heart disease → fear of death → beginning of dyspnea on exertion and anxiety symptoms	Overprotection by mother, ambitions shattered, fear of death (at age 5) after cousin's death from heart disease
4	26, C, M, rheumatic heart disease with mitral stenosis and insufficiency, class 1	Undetermined	Probable: loss of bowling match → development of pulmonary edema immediately afterward	Knowledge of relation between physical exertion and heart disease → fear of work; medical support and reeducation → full employment
5	66, C, F, arteriosclerotic heart disease, class 3	Undetermined	Undetermined	First serious illness in patient's life, fear of death or crippling infirmity
6	52, C, F, lupus erythematosus with associated carditis, class 1	Undetermined	Questionable: death of father → ambivalence about returning home to care for mother → CHF symptoms and also signs of lupus erythematosus	Patient was mainstay in large family, position she held reluctantly; guilt about shirking duty
7	69, C, M, arteriosclerotic heart disease, class 3	Undetermined	Undetermined	Life of hard and devoted work with "nothing" to show for it, resented wife's supporting him
8	50, C, M, rheumatic heart disease with mitral stenosis, class 2	Wife did not accept illness and chided him about unmanliness → patient attempted to prove strength and continue excessive physical exertion (e.g., mowing lawn)	Definite: Coitus followed by increased dyspnea only when patient and wife at odds	Continuing strain between patient and wife
9	60, N, M, hypertensive heart disease, class 2	Denial of illness → ambivalence and guilt about caring for invalid wife → continued farming → perpetuation of CHF	Undetermined	Dependency unacceptable, work demands precluded adequate rest, invalid wife, emotional and financial deprivation
10	40, C, F, rheumatic heart disease with mitral stenosis, class 2	Feeling of duty to church and minister → overexertion working for minister	Definite: anxiety about illness of son and fear of losing him→ exacerbation of CHF	Husband's illness, hostile dependency on husband
11	54, C, M, arteriosclerotic heart disease, class 2	Undetermined	Questionable: argument with client while working as hotel clerk → brief exacerbation of symptoms	Emotional outlets of sexual promiscuity and wandering limited by illness, separation from family → loneliness
12	50, C, F, rheumatic heart disease with mitral stenosis, class 2	Fear of dependency and loss of capacity to work → denial of illness → continued work in factory → perpetuation of CHF	Questionable: developed CHF symptoms after emotionally traumatic operation	Illiterate, frigid, sterile
13	50, C, F, arteriosclerotic heart disease, class 1	Undetermined	Undetermined	After husband's death raised five children now grown, marital conflict with second husband
14	52, C, M, arteriosclerotic heart disease, class 1	Undetermined	Probable: move to strange town and loss of position → decompensation → regained position → compensation without change in medical regimen	Undetermined
15	78, C, F, hypertensive and arteriosclerotic heart disease, class 2	Undetermined	Definite: marital dispute in family next door aroused intense feelings of identification with the wife → decompensation → hospitalization → immediate compensation	Dissatisfaction with move from home made necessary by illness

*Age, race (C=Caucasian; N=Negro), sex, diagnosis, and functional class.

Chambers and Reiser,[11] making a special effort to determine significant emotional stresses correlating with the precipitation of congestive failure, studied 25 consecutive patients admitted to a general hospital with this diagnosis. In 23 of these patients precipitating factors were identified, and in 19 "it was felt that emotional tension was the factor immediately responsible for increasing the work load beyond cardiac capacity." Five patients were treated by the same internist for an extended period, and there was relative stabilization in the clinical condition of four. Commenting on these five patients the authors stated, "The clinical response appeared to be determined, in large part, by the degree and nature of the dependency on the physician." In two patients the departure of the physician was followed by exacerbation of failure.

Comparison of these three clinical studies indicates (*a*) a discrepancy in the proportion of instances in which precipitating factors were identified and (*b*) a discrepancy in the proportion of instances in which emotional factors were regarded as significant in the precipitation of heart failure. In the first two series no precipitating factors were determined in almost half the patients (486 of 1,100), whereas in the third series precipitating factors were determined in over 90% of the patients (23 of 25). In addition, emotional or psychic factors were discovered and regarded as significant in only 3 of 1,100 patients reported in the first two series (0.27%) but in 19 of 25 in the third (80%). The data presented in this report may be relevant to these discrepancies.

Synopses of Thirty Cases of Congestive Heart Failure (CHF)—Continued

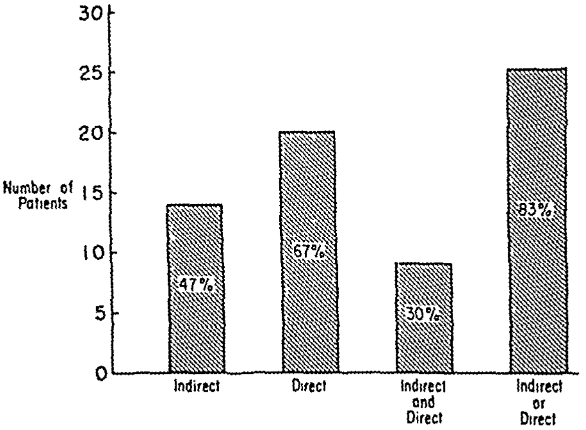
		Emotional Influences		
Case No.	Patient Data*	Acute Indirect	Acute Direct	Chronic
16	61, C, M, hypertensive and arteriosclerotic heart disease, class 4	Fear of failure and dependence → continuation of excessive work → perpetuation of CHF	Definite: demoted from principal to teacher and relocated → emotional stress of teaching → precipitation of CHF	Constant emotional strain of work, leaving a long-time home
17	71, C, M, hypertensive and arteriosclerotic heart disease, class 4	Undetermined	Undetermined	Feeling of loneliness and relative hopelessness since death of wife, resigned to own death, disappointed in children
18	68, C, M, hypertensive and arteriosclerotic heart disease, class 3	Felt indispensable on farm → resentment about farming which he disliked, feared accepting enforced dependency → denial of illness → failure to accept medical care → perpetuation of CHF	Questionable: resentment toward mother who kept him on farm aroused by illness and fear of dependency → perpetuation of failure (resentment often transferred to doctors)	Frigid wife, loss of farm work as means of relieving anxiety
19	48, C, M, rheumatic heart disease with mitral stenosis, class 3	Undetermined	Definite: auto accident → anxiety → exacerbation of CHF	Unusually well adjusted to illness
20	70, C, M, arteriosclerotic heart disease, class 3	Lonely since wife's and sons' deaths and "need" to work → denial of illness → lack of medical supervision and continuance of work → perpetuation of CHF	Questionable: increase in CHF symptoms after accidentally killing son	Charged with murder of son, lonely since death of wife, death of another son in auto accident
21	18, C, F, rheumatic heart disease with mitral stenosis, class 1	Fear of death or mutilation → refusal of operation for relief of mitral stenosis → continuance of mild CHF	Probable: cardiac catheterization → fear of death → anxiety → transient dyspnea	Generally well adjusted, illness mild and not a drastic interference
22	47, C, F, arteriosclerotic heart disease and myxedema, class 4	Undetermined	Undetermined	Sterility problem, father's death (patient aged 6) and consequent need to assume adult chores early
23	23, C, M, rheumatic heart disease with multiple valvular disease, class 4	Undetermined	Questionable: continued preoccupation with unpleasant experience (assault by drunk) → one month later developed congestive heart failure with anasarca	Low intelligence, sexual problems, fear of illness
24	63, C, M, arteriosclerotic heart disease, class 3	Undetermined	Questionable: first exercise after myocardial infarction → slight dyspnea → fear of another infarct → development of peripheral edema in one-half hour	"In love" with work, work precluded by CHF, wife frigid and distant
25	24, C, M, rheumatic heart disease with multiple valvular disease, class 1	Undetermined	Definite: having to study while in school, conflict with dependency wishes → anxiety → transient dyspnea	Good general adjustment to illness
26	47, N, M, hypertensive heart disease, class 3	Demands of family and farming → denial of illness → continuance of work and failure to accept medical regimen → perpetuation of CHF	Undetermined	Frigid wife, nine children, loss of ability to work since illness
27	38, C, M, hypertensive and arteriosclerotic heart disease, class 3	Obesity (overeating for gratification and relief of anxiety) → denial of illness since it took away eating defense → off diet → exacerbation of CHF	Undetermined	Single man with no close relationships, chronic emotional "hunger"
28	46, C, M, rheumatic heart disease, class 3	Need to work for living and to relieve anxiety → denial of illness → overexertion → perpetuation of CHF	Definite: inactivity (work only means of gratification) → restlessness and anxiety → transient episodes of dyspnea	Lack of interpersonal gratification, loss of work as means of relieving tension
29	53, N, F, arteriosclerotic heart disease and tuberculosis, class 3	Need to care for others → neglect of own illness (denial) → exacerbation of CHF	Undetermined	Poverty and need to support family
30	54, C, M, hypertensive heart disease, class 3	Undetermined	Undetermined	Total repression of emotional responses, intractable hypertension

*Age, race (C=Caucasian; N=Negro), sex, diagnosis, and functional class.

In the course of a series of studies of the influence of emotional factors on congestive heart failure, particularly as these relate to changes in peripheral [4c] and central venous pressure,[4d] a group of 30 medical patients were interviewed by the psychiatrist (C. R. V.).

Method and Results

The patients were selected on the basis of availability and not because of primary psychiatric disorder. They were interviewed initially for one to two hours either on the wards or in the outpatient department of the North Carolina Memorial Hospital. The progress of five patients was followed regularly for 3 to 15 months. A relatively unstructured interview was used, and in many instances the interview was tape recorded. An effort was made to gather historical data about the patient's total life adjustment, techniques of dealing with interpersonal problems, and instances of breakdowns in adjustment, either in the form of "medical" illness or in the form of some behavioral, affective, thinking, or psychophysiological disturbance. Attention was paid to assessing the situations likely to be difficult for each patient, since, as Wolf [12] emphasized, determining the specificity of the symbolic meaning of the life situation for the individual may be essential. Of these 30 patients 12 also participated in the previously mentioned laboratory studies.[4d]



Frequency of emotional influences on precipitation or exacerbation of congestive heart failure in 30 patients.

Previous work by us [4d] has indicated that it is possible for a physician in the course of taking a medical history to identify disturbing life situations and emotional experiences related to exacerbations of congestive heart failure and to predict, at the 5% level of confidence, their effect in increasing central venous pressure. The present report is concerned, however, not with the quantitative aspects of these studies but rather with their qualitative features.

For purposes of clarity, emotional or psychological factors were considered to be related to the precipitation or perpetuation of congestive heart failure directly or indirectly, or both. Although this is an arbitrary distinction there are practical advantages in making it. The patient data are summarized in the table, and the distribution of direct and indirect influences is indicated graphically in the figure. Five patients (30%) had both direct and indirect factors present, and 25 patients (83%) had either direct or indirect factors present.

Report of Cases

Indirect Influences.—Patients may respond indirectly to specific life situations, or to the presence of heart disease itself, by physical overexertion, failure to take medicaments, or refusal to follow dietary restrictions. Psychological problems which complicate the understanding or successful implementation of treatment regimens were regarded as indirectly deleterious effects. These indirect influences were discovered in 14 patients in this series of 30 (47%).

Case 18.—This 68-year-old farmer was unable to accept the fact of his heart disease and refused to continue an adequate medical regimen. Previously latent mixed feelings were aroused after his heart disease began or became manifest, which seemed to arise from having devoted most of his life to farming, in response to his mother's wishes, in opposition to his ambition to leave the farm and work in the city. He resented the imposition of his disease and attempted to deny its presence; not accepting his disease and the dependency it demanded, he would neither take his medicaments regularly nor remain on a diet, and his failure persisted and was regarded as "intractable."

This patient demonstrates the obligatory use of the mechanism of denial in the face of life-threatening, but not necessarily fatal, organic disease. Denial may be seen to some degree in most patients with a serious illness, but its use at the expense of accepting appropriate treatment indicates unusually intense underlying psychological conflict evoked by the illness itself. In this instance the unresolved mixture of both positive and negative feelings toward the patient's mother was identified as part of his underlying conflict.

Direct Influences.—In 19 patients (63%) emotional factors appeared to be involved more directly in the precipitation or perpetuation of congestive heart failure. In seven a definite relationship between the emotionally disturbing life situation and the development or exacerbation of failure symptoms was established, in five instances a probable relationship was established, and in seven the relationship was questionable. In 3 of these 19 patients the effect of the disturbing situation on the cardiovascular status was definite but transient, lasting only a few minutes to a few hours (see table, cases 3, 5, and 6). The precise mechanisms through which these emotional influences act are not clear, but available evidence suggests that affects and associated neurochemical changes are directly involved in the regulation of cardiovascular function. In 26 of 30 patients (87%) chronic emotional tension arising out of unresolved interpersonal conflicts seemed important in precluding an adequate over-all psychological or physiological adjustment to the presence of organic heart disease.

Case 4.—This 26-year-old electrician's helper knew he had rheumatic heart disease but would not allow himself to be impressed by his physical impairment, although he had had one previous attack of pulmonary edema. At times, however, this denial mechanism was inadequate. For example, he was inordinately enthusiastic about physical exercise and engaged in many sports, of which bowling was of current interest. One evening after bowling he developed dyspnea and frank pulmonary edema. Superficially it appeared that physical exertion had precipitated this episode. On the other hand, he had been bowling many times that week without difficulty. Closer examination revealed that on this night his team was bowling for the championship. He was admittedly excited and concerned about the possibility of losing. His team did lose and, as he stated later, "I took the game home with me." He noticed shortness of breath only after reaching home that evening. The more he ruminated about his bowling match the more his dyspnea increased, and by the next morning he had developed pulmonary edema, necessitating immediate medical attention. After hospitalization and appropriate treatment symptoms of failure receded, and he was relatively free of symptoms related to the failure itself.

After this recovery, however, he had recurrent precordial discomfort of a vague and ill-defined nature. Fearing further trouble he resisted surrendering the protection and gratification of his dependency needs given him as long as he was ill. During the course of four 15-to-30-minute interviews with him certain problems were clarified, including his extreme anxiety about heart disease, his previous successful and later unsuccessful denial of his heart disease, and his ignorance of the various problems involved. As these matters were brought out and discussed the symptoms abated and he returned to full employment, continuing regular visits with his local physician.

This case demonstrates the prominent role anxiety may play in the sequence of events accompanying the development of pulmonary edema. Physical exertion with tachycardia presumably was an important contributory, perhaps dominant, factor in initiating the syndrome; but persistent anxiety, through either further tachycardia or other mechanisms, appeared to make his recovery from the evening's physical exertion impossible. The anxiety seemed related to earlier childhood experiences concerning the problems of competition and failure. Once the acute situation had been relieved, effective rehabilitation became a threat to him until (*a*) continuing support even after the acute attack was acknowledged by the physician as needed, (*b*) the nature and degree of his illness were discussed with him, and (*c*) he was given a chance to adjust to it.

Case 8.—This 50-year-old man described a situation similar to that of the preceding patient. Dyspnea, in this instance, developed during a baseball game in which he was neither playing nor exerting himself physically but was coaching the team on which his son was playing and had a substantial emotional investment in the game.

There were other direct adverse influences on him. At times during sexual intercourse he developed severe dyspnea from which he would recover in several hours. It was clear in his mind that, when he was relaxed, copulation, even prolonged, was not followed by dyspnea. However, when he was tense, he would become excessively dyspneic in a short time. In discussing with him his marital relationship he revealed varying degrees of tension between himself and his wife relating to her extramarital sexual escapades in the past. His resentment toward her was ordinarily hidden and they maintained a distant emotional relationship much of the time. When their lives were not complicated by the arousal of this conflict, no dyspnea developed during sexual relations; however, when this emotional conflict was evoked dyspnea developed during intercourse. A further complicating indirect influence in this case was the wife's attitude toward the patient's illness. Noting his healthy appearance and not appreciating his disability she belittled his heart disease. He avoided discussing this with her. As a result he felt the need to continue doing physical work far beyond his capacity, e. g., mowing the lawn.

The adverse effect on cardiac compensation resulting from the interplay of physical exertion and emotional conflict is again illustrated by this patient. Physical exertion in itself may not lead to more than temporary dyspnea, but with the added burden of emotional tension aroused in interpersonal conflict clinical symptoms may become manifest, especially when rest and relaxation are precluded by continuing tension.

Case 14.—This 52-year-old successful factory worker had worked his way up to a superintendent's job. He was persuaded by his employer to go to another state and help develop a new plant. Although assured of a good position at this new factory he was demoted shortly after arrival. This demotion questionably entailed a slight increase in physical exertion. When a friend who was personnel manager at this new plant died, he felt helpless and without hope for regaining his old position. His local employer threatened him when the patient suggested complaining to higher officials in the company about the situation. Further feelings of helplessness and a sense of being "trapped" were soon followed by dyspnea, weakness, and substernal oppression. The situation seemed to be a recapitulation of his feelings about his father's death, which occurred when the patient was 14 years of age; as on that occasion, he felt lost and abandoned.

Physical findings, the electrocardiogram, and results of x-ray studies corroborated a diagnosis of coronary artery disease with congestive failure. He was placed on the usual medical regimen of digitalis and a low-salt diet and was advised to limit his activities, but the congestive failure persisted. Situational factors related to his work were known to his physician. but since the plant director had warned the patient not to expose the matter the physician was not able to alter the situation in any way except to advise him to rest and limit his activities. A change of jobs was impracticable at his age, even though he was quite able to work and was aware of this. He was referred to the North Carolina Memorial Hospital, where, without significant changes in medical therapy, he recovered, and only minimal signs of heart disease were demonstrable. In the meantime, while he was in the hospital, company officials became aware of the local situation in the plant and soon cleared it up, and he returned to his old job, free of symptoms.

A combination of possible increase in physical exertion at his job, the associated blow to his self-esteem, and arousal of the separation anxiety associated with the death of his father were the apparent cumulative forces which precipitated congestive failure in this patient with minimal organic heart disease.

Case 21.—This 18-year-old high-school student had one episode of pulmonary edema apparently associated with an infection. During cardiac catheterization she developed dyspnea. It was an overwhelmingly frightening situation for her, and she was aware of the reduction of symptoms during the course of the procedure when she was diverted and encouraged by one of the physicians.

Case 25.—This 24-year-old theological student was relatively free from dyspnea during most of his life. However, with moderate physical exertion he developed some dyspnea. In addition, under circumstances of emotional tension related to a conflict about studying versus not studying, he would often notice dyspnea.

In neither of these latter two examples was the emotional component of the total adjustment important at the time of examination. They are examples of the temporary effect of certain anxiety-provoking situations on cardiovascular function. It might be postulated that with further decrease in cardiac reserve, emotional conflicts would assume a relatively more important role in symptom formation.

Case 1.—A 58-year-old mill-worker gradually developed severe congestive failure over a nine-year period. A myocardial infarction was the initiating episode. After the infarction he had repeated episodes of chest pain and gradually developed congestive failure with occasional attacks of angina pectoris. During this time he had one transient cerebrovascular accident. His previous physical health had been excellent, and he prided himself on his physical prowess in fights and on his excessive drinking. His fondest memories were of the days when he was in the armed service where he enjoyed many "drunken brawls." Although winning was an important issue to him, the crucial matter was the struggle itself. As long as he put up a good fight, losing did not concern him greatly. His drinking and fighting did not interfere drastically with his general adjustment, since he maintained an excellent work record as well as a surprisingly stable marriage and family, but seemed to be his way of resolving the conflicts which developed out of his never having had a father, since the latter left home when the patient was 3 weeks old. Furthermore, he was brought up in an environment with substantial material deprivation. He had a strong and apparently healthy relationship with his mother, and although she expected a great deal of work from him he was able to keep up with it, taking pride in his work capacity. He worked in a cotton mill from the age of 11 years, except for two "hitches" in service, one in the Army and one in the Navy. His record in the mill was good, and for many years he was chief electrician. However, during the five years prior to his heart attack the work at the mill became increasingly demanding, because of a change in the management. The harder he worked the more work was expected of him, and he began to feel that the amount expected exceeded his ability, particularly during the year preceding his heart attack.

The heart attack was understandably an overwhelming blow to his self-esteem, taking away two of his psychological defense mechanisms, drinking and fighting. From a "healthy" adult he was transformed into a helpless child. The ensuing years were fraught with alternating periods of helplessness when he was in a state of decompensation and periods of relatively good health. He had repeated attacks of congestive failure, saw numerous physicians, and was hospitalized many times. He could never accept caloric or salt restrictions. After hospitalization in October, 1956, he was seen regularly in the North Carolina Memorial Hospital outpatient department by the same physician. After much discussion during the course of his weekly visits to the medical clinic (approximately 20-minute interviews after the initial evaluation) he began to see his disease as an "enemy" and to deal with his illness in the same way that he might attack an adversary. Dietary restrictions became a challenge, and he accepted them as such with enthusiasm. From the beginning, when he revealed the nature of his internal struggle, each visit with the physician consisted primarily of a discussion of tactics and strategy as to the best way for him to "fight" his disease. As a result he became an expert on his condition and, although remaining greatly limited in activity, learned to recognize his limitations and to deal realistically with his physical status. Psychologically, he seemed to use his physician as an ally and expert consultant, who helped him plan and carry out his fight with the heart disease successfully.

During the course of this follow-up he had an episode of failure after an older brother's death from heart disease. This brother was a particularly important figure in his life, representing the one to whom he looked for guidance. He had followed closely in his brother's footsteps during his life. In the succeeding several weeks while he mourned his brother's death he gained weight, became increasingly dyspneic, and finally developed an upper respiratory infection, bronchial pneumonia, and progressive signs and symptoms of heart failure. Some dietary indiscretions were suspected as well during this progressive course. Hospitalization and appropriate medical attention were followed by prompt remission.

This case illustrates the complexity of the psychophysiological picture of the patient with congestive failure. In the course of medical follow-up visits information was gathered about the patient's personality adjustment, his ways of dealing with anxiety, especially anxiety aroused by the enforced dependency of his illness, and the interplay of these with his cardiovascular status. Medical management in the form of drug administration, dietary alterations, and activity limitation became much simpler to carry out in the light of knowledge gained about his interpersonal and intrapsychic reaction patterns. This could only be done in the setting of a continuing doctor-patient relationship.

Comment

From the foregoing data it is inferred that the emotional state of the individual may provide important clues to understanding the many-faceted maladjustments which characterize the syndrome of congestive heart failure. Intrapsychic mechanisms, e. g., denial, may mask the underlying tension consequent to interpersonal conflict arising during illness or evoked as a result of the presence of illness. Many other variants of intrapsychic reactions and emotional responses may be expected in patients with a chronic illness like congestive heart failure; this is not surprising in view of the profound part the cardiovascular system plays in the development and organization of man's unique capacity for symbolic language. Symbolically the heart retains its sovereignty over emotions, as Aristotle has taught. This is exemplified by its use in manifold ways in literature and everyday language as the "core" of emotions. Also, colloquial expressions reflecting reactions to life associated with the heart are numerous; e. g., "I almost had a heart attack," or "it gave me heart failure." Complicating disturbances of the whole organism may be expected when there is lack of harmony between the functioning of the heart and the needs of the organism for total adaptation or, as Schneider[13] put it, "dys-energy between the image of the heart and the rest of the ego."

The data herein presented are in accord with the findings of Chambers and Reiser[11] and support their conclusion that "emotional stress is a frequent precipitating factor in the development of congestive heart failure in the patient with limited cardiac reserve."

Once congestive heart failure has developed the physician seeks ways to increase the efficiency of the heart and decrease its load. Etiological, anatomic, and functional diagnosis of the underlying heart disease is a prerequisite, but available evidence now suggests that an understanding of the personality of the patient and the circumstances in which the illness developed is of equal importance. To facilitate the attainment of optimum cardiovascular compensation the patient will need support in making an over-all adjustment to his life situation. Some practical considerations for planning the management of patients with congestive heart failure which may be derived from this study follow.

1. Impairment of cardiovascular function evokes a signal of danger—anxiety—which is usually useful but may be emotionally disturbing and psychologically deleterious. The physician relieves this anxiety, first by accepting responsibility for identifying the failing heart as the source of danger and second by instituting a medical regimen to increase the heart's efficiency and to decrease its work load.

2. Congestive heart failure, like other chronic disease, arouses dependency needs, which are biologically determined "calls for help." In certain patients these may be unusually strong and infantile, so that their emergence threatens the individual who has a need to repress dependency longings as a result of early childhood conditioning. The physician accepts, indeed may demand, the patient's dependency on him. At first he may take virtually full responsibility for the patient's care; later they share this burden.

3. Dependency (i. e., need to be cared for) gratification during the acute stage of the illness may be difficult for some patients to relinquish after relative compensation is established. The physician allows for some dependency while at the same time supporting a realistic rehabilitation program.

4. Additional sources of anxiety may be evoked when latent interpersonal conflicts become abruptly manifest or develop during the course of illness. The physician may use his relationship with the patient as a means of understanding the patient's emotional life and the specific sources of conflict. Furthermore, he is a source of strength and support (in psychiatric terms; an ego surrogate) for the patient to use while his own strength is depleted by illness.

5. Fear of the unknown is a special concern to most patients. By explanation and amplification the physician carefully helps the patient educate himself about his illness. The two work together in learning the peculiarities of the individual, his illness, and his new life with the illness.

The utilization of this approach to the management of patients with congestive heart failure is nothing new in the practice of medicine. The intuitive application of these principles is time-honored. However, in the light of present, more precise knowledge of how the human organism operates psychosocially, as well as physiochemically, a beginning toward more rational understanding of patient management becomes available.

Summary

In the course of other physiological studies 30 patients with congestive heart failure were studied by a psychiatrist, with particular reference to their emotional responses to cardiac failure. Fourteen patients (43%) were found to have indirect and 19 patients (63%) direct deleterious emotional responses precipitating, aggravating, or perpetuating congestive heart failure. In 9 patients (30%) both influences were present and in 25 patients (83%) either direct or indirect influences were present. Management of the patient with congestive heart failure should make use of data about the patient, his personality, and the circumstances under which his illness developed.

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ADVERSE EFFECTS OF SMOKING DURING PREGNANCY—Obstetrical and smoking histories were recorded for 2,042 pregnant women delivered in six Birmingham maternity hospitals during the summer of 1958. The mean weight of infants of mothers who smoked regularly throughout pregnancy was 6 oz. (170 g.) less than that of infants of mothers who never smoked during pregnancy (6.93 lb. and 7.33 lb. respectively). This was more than the difference in weight between male and female infants and between first and later births. It was sufficient to lower significantly the incidence of surgical induction among smokers. . . . If the effect of smoking on birth weight is as considerable as this inquiry indicates, it is evident that it must make a substantial contribution to the frequency of "premature births," defined according to weight.—C. R. Lowe, M.D., Ph.D., D.P.H., Effect of Mothers' Smoking Habits on Birth Weight of Their Children, *British Medical Journal*, Oct. 22-25, 1959.

PROMETHAZINE DRIP IN THE POSTOPERATIVE MANAGEMENT OF SUPRAPUBIC PROSTATECTOMY

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The danger of extravasations of blood and urine after suprapubic prostatectomy is increased in patients made restless by pain and by reflexes arising from the region of the bladder. Prolonged, heavy sedation with narcotics alone is undesirable in elderly patients. The possibility that better results might be obtained by administering a combination of a narcotic and promethazine hydrochloride was investigated in 82 patients who had undergone suprapubic prostatectomy under spinal anesthesia. All received meperidine or morphine as needed for pain. Patients in group 1 (41 patients) in addition received promethazine by intravenous drip; those in group 2 (34 patients) received no promethazine; and those in group 3 (7 patients) received promethazine intramuscularly. Patients in group 1 remained free from nausea, vomiting, chills, and cold sweats; tolerated postoperative bladder irrigations without reflex spasms or hemorrhages; and required, on the average, less than half the dose of narcotics required in group 2. No untoward effects were observed.

Among the major difficulties associated with suprapubic prostatectomy is the immediate postoperative period, which is often characterized by pain and straining on the part of the patient and a subjective sensation of tenesmus. These are usually attributable to the necessity for prostatic packing, tube devices, and sometimes actual traction, which provoke an overwhelming desire to void. The ensuing agitation and violent attempts to expel the foreign bodies residing in the bladder may cause activation of bleeding and autonomic imbalance. Postoperative hemorrhage and straining can result in the extravasation of urine and blood into tissues surrounding the prostatic bed. This in itself can be extremely dangerous. To alleviate the resultant discomfort, reliance has hitherto been only on the use of narcotics, and high dosages of these, as is well known, can be disastrous for elderly patients.

The duty of the surgeon-urologist *certainly does* not end with the completion of the prostatectomy. Also, the responsibility of the anesthesiologist cannot be considered to end with the technical completion of the operation. Postoperatively, the surgeon and the anesthesiologist must continue to work as a team to understand the requirements of the patient and to alleviate whatever postoperative complications occur.

The object of this study was to discover a method by which patients could be maintained in a state of slumber, free from pain and reflex spasms, during a 24-hour postoperative period.

Originally, promethazine (Phenergan) hydrochloride, a phenothiazine derivative, was administered in conjunction with the narcotics prescribed postoperatively. The patients appeared to exhibit an *increased response to the narcotics employed,*[1] and the time interval between required doses could be increased, that is, a narcotic which normally would have been administered every four hours could be administered every five or six hours. It had also been observed that promethazine hydrochloride, in addition to its ability to potentiate the effects of the narcotic agents,[2] also possessed tranquilizing and sedative properties.[3] It was decided, therefore, to administer promethazine hydrochloride by the intravenous drip method to determine the efficacy of the agent when it was given in this manner.

Method

A total of 82 patients, ranging in age from 49 to 81 years (average age, 66.3 years), who had undergone suprapubic prostatectomy procedures were included in this study. Of the 82 patients 75 were grouped according to the medicament received. Group 1 included 41 patients who were given promethazine hydrochloride by the intravenous drip method postoperatively and narcotic agents as required. Group 2 included 34 patients who were not given promethazine in any form postoperatively but who did receive narcotic agents as required for the relief from pain. The remaining seven patients received, in addition to the narcotic agents, promethazine hydrochloride by injection in order to confirm the results obtained in previous studies of patients who were given promethazine postoperatively.[3]

A combination of either two or three of the following agents was given as premedication to the 82 patients: atropine, from 1/150 to 1/100 grain

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(0.4 to 0.6 mg.); meperidine, from 25 to 100 mg.; promethazine, from 25 to 50 mg.; scopolamine, from 1/150 to 1/100 grain; diphenhydramine, 10 mg.; pentobarbital, 155 mg.; and morphine, from ⅛ to ¼ grain (8 to 15 mg.).

Spinal anesthesia was selected as the anesthetic procedure in all the suprapubic prostatectomies for two reasons: (1) to obtain muscular relaxation without postoperative nausea and vomiting and (2) to enable careful observation of the effect of the promethazine drip without the superimposed depressant action of anesthetic agents.

For the patients in group 1 the promethazine hydrochloride was added to an infusion and administered intravenously. Initially the dose was 50 mg. per 1,000 cc. of fluid employed. The drip was permitted to run at a rate of 40 drops per minute and was increased or decreased according to the response of the patient. Later, the dose was stabilized at 75 mg. of promethazine per 1,000 cc. of solution, given at a rate of 30 drops per minute for a period of from 12 to 16 hours. The method employed was to administer a total of 150 mg. of promethazine per 2,000 cc. of solution. The promethazine drip was not started until the patient was in the postoperative recovery room; however, when the patient was in pain, narcotic agents were not withheld. Patients who undergo suprapubic prostatectomy procedures must have special nursing care for at least the first 24 hours postoperatively. For this reason, careful supervision and observation of the effects of the use of the promethazine hydrochloride drip method were possible.

*Units of Narcotic Agents Required Postoperatively by Patients in Groups 1 and 2**

	Group 1		Group 2	
Narcotic Agent	Units	Patients, No.	Units	Patients, No.
Meperidine	1.00	5	1.50	1
	1.50	4	2.00	2
			2.25	4
			2.50	1
			2.75	1
			3.50	1
			3.75	1
			4.00	1
			4.25	1
Morphine	1.00	3	2.00	2
	1.50	1	3.00	4
	1.67	1	4.00	2
	2.00	2		
Meperidine and Pantopon (opium alkaloids)	1.00	1	3.50	1
	1.75	1		
	2.50	1		
Morphine and meperidine	1.00	1	3.00	1
Total	54.00	41	102.75	34
Av. dose per patient	1.32		3.02	

* Units are narcotic equivalents: meperidine, 100 mg.; morphine, ¼ grain (15 mg.); and opium alkaloids, ⅓ grain (20 mg.).

Results

With the concentration of promethazine used in the intravenous drip (150 mg. per 2,000 cc.) the patients were less restless and were maintained in a state of light slumber from which they could be aroused at will. Although the patients were awakened by irrigations of the bladder, these were easily tolerated and did not cause any reflex spasm. Postoperative hemorrhage, activated by the straining and pushing of unruly patients, did not occur. No decrease in blood pressure was observed. Respiratory depression, nausea, and vomiting were absent,[1] and the "chills" and "cold sweats," which were frequently experienced by patients in the past, did not occur in a single patient in group 1. Symptoms of intestinal or vesical autonomic imbalance did not develop in any of the patients who received the promethazine by the intravenous drip method. The number of narcotic units[4] required by patients in groups 1 and 2 is shown in the table. The 41 patients who received promethazine hydrochloride by the intravenous drip method (group 1) required fewer narcotic units[4] for the alleviation of pain. In group 1 the total number of units required for all 41 patients was 54, and the average was 1.3 units per 24-hour period per person. In group 2 the total number of units required for the 34 patients was 102.75, an average of 3.02 units per 24-hour period for each person. Not only was the amount of narcotic agents required decreased for the patients in group 1 but the time interval between doses was increased.

The results obtained for the seven patients who received promethazine hydrochloride by intramuscular injection confirmed the results noted in earlier studies and those procured by other investigators.[3] It was clear that a smaller amount of narcotics was necessary when promethazine was given in conjunction with the narcotic intramuscularly, with an average of 2.5 narcotic units. This was greater than the amount of narcotics required when promethazine was administered by the drip method.

Summary and Conclusions

The use of promethazine hydrochloride, administered to 41 patients by the intravenous drip method, proved to be the greatest aid in satisfactorily sustaining the patients during the 24-hour postoperative period after suprapubic prostatectomy procedures. It is believed that the method is a valuable aid in the postoperative management of any patient who must undergo a traumatic operation and who is in an age group in which the best physiological conditions do not prevail. The reduction in the amount of narcotic agents required is, in itself, extremely advantageous, when it is considered that the administration of narcotics alone can be disastrous for elderly patients. Other advantages of the promethazine drip are the tranquility achieved and the elimination of undesirable autonomic reactions. No untoward side-reactions were observed.

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ISOLATION OF ENTEROPATHOGENIC ESCHERICHIA COLI FROM HOUSEHOLD PETS

RELATION TO INFANTILE DIARRHEA

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Good evidence has accumulated pointing to enteropathogenic Escherichia coli as a cause of infantile diarrhea. During the course of this one-year bacteriological investigation, Esch. coli were isolated from 321 household pets, 237 dogs and 84 cats that were apparently healthy. Rectal smear specimens were obtained in the study through the cooperation of veterinarians and families. A higher percentage of positive cultures was obtained during the summer months. Epidemiologic study in the case of an 11-month-old infant hospitalized for gastroenteritis revealed that a dog in the household was the specific source of infection.

At the present time good evidence has accumulated pointing to enteropathogenic Escherichia coli as the cause of infantile diarrhea. The etiological significance of this type of epidemic infantile enteritis is proved on the bases of bacteriological, clinical, epidemiologic, pathological, and therapeutic results. Bray,[1] Kauffmann and Dupont,[2] and Ferguson and co-workers[3] made feeding experiments of two serotypes of Esch. coli to adult volunteers who ingested Esch. coli $0111:B_4$ strain and developed serum agglutinins for the organism. Some who did not show any symptoms developed agglutinins to some degree. On the other hand, no volunteer developed a rise in agglutinin titer for the normal coliform organism. These serotypes of Esch. coli have been recovered from the feces, nasopharynx, and throats of random patients with infantile diarrhea by Neter.[4] In his findings he showed that contact with the multiplication of these serotypes of Esch. coli may be followed by an attack of diarrhea, indicating that these organisms may be considered as a cause of this disease.

I originally isolated Esch. coli type strains from newborn calves with white scours. I differentiated these strains by their fermentative properties in relation to various sugars and named them Esch. coli types. Later Orskov[5] isolated Esch. coli strains belonging to O group 26 from patients with infantile enteritis and from newborn calves with white scours. He established one serologic type $26:B_6:11$ and two biochemical types. Fey[6] reported on two new Esch. coli serotypes belonging to O group $55:B_5:8$ and $55:B_5:10$. The first type was isolated from a chicken and from a patient with infantile enteritis and the second type from the sperm of a bull. He has reported on the occurrence of Esch. coli serotypes of O group 26, 55, 86, and 0111 in animals and on coliform bovine mastitis with special reference to infantile enteritis.

Materials

As bacteriological examination of fecal specimens from household pets, i. e., dogs and cats, was the most important part of this study, arrangements were made with veterinarians and owners of pets to have the specimens collected, in the form of rectal swabs. Swabs in 3% glycerine in saline solution were prepared and supplied to the veterinarians and owners of pets. It was noted that this method of collecting rectal swabs facilitated the procedure for handling the specimens.

Isolation Mediums.—Since Esch. coli serotypes usually do not grow on the highly selective mediums in general use for the isolation of Salmonella and Shigella, less inhibitory differential mediums such as

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MacConkey's and eosin-methylene blue agar were employed. In addition to the differential plating mediums a blood agar plate was streaked with a small inoculum of fecal specimen, because it has been noted that in a few instances Esch. coli serotypes 0111 and 055 are not hemolytic, a fact which may aid in the recognition of colonies; however, undue reliance was not placed on this observation because many other Esch. coli serotypes are hemolytic, and it is possible that hemolytic variants of Esch. coli 0111 and 055 and of other serotypes associated with infantile diarrhea exist.

TABLE 1.—*Summary of Biochemical Reactions of Eighteen Strains of Esch. Coli 026:B_6 Isolated from Household Pets*

Strains	1	2	3	4	5	6	7 to 18
Serotypes	026:B_6	026:B_6	026:B_6	026.B_6	026'B_6	026:B_6	026:B_6
Reaction, Type							
Adonitol	—	—	—	—	—	—	—
Dulcitol	+	+	+	+*	+	+	+
Sorbitol	—	+	+	+	+	+	+
Arabinose	+	+	+	+	+	+	+
Xylose	+	+	+	+	+	+	+
Rhamnose	—	+*	+	—	+	—	—
Maltose	+	+	+	+	+	+	+
Salicin	+*	+	+	+*	+*	+*	+
Inositol	—	—	—	—	—	—	—
Lactose	+	+	+	+	+	+	+
Sucrose	+	+	+	+	+	+	+
Sorbose	+	+	+	+	+	+	+
Mannitol	+	+	+	+	+	+	+
Glucose	+	+	+	+	+	+	+
Indole	+	+	+	+	+	+	+
H_2S	—	—	—	—	—	—	—
Gelatin	—	—	—	—	—	—	—
Ammonium citrate	—	—	—	—	—	—	—
Potassium nitrate	+	+	+	+	+	+	+
Voges-Proskauer	—	—	—	—	—	—	—
Methyl red	+	+	+	+	+	+	+
Urea	—	—	—	—	—	—	—

*Delayed reaction.

Esch. Coli Serotype Antiserums.—Esch. coli serotype antiserums, which are highly titered absorbed antiserums prepared from strains of enteropathogenic Esch. coli associated with infantile diarrhea, were obtained commercially. The 10 recognized serotypes were divided into two groups: group A, comprising those most frequently encountered, consisted of serotypes 011:B_4, 055:B_5, 0127:B_8, and 026:B_6, and group B consisted of serotypes 086:B_7, 0119:B_{14}, 0124:B_{17}, 0125:B_{15}, 0126:B_{16}, and 0128:B_{12}. Two polyvalent OB antiserums were available. Esch. coli OB antiserum polyvalent group A is a mixture of the more commonly encountered Esch. coli serotypes listed in group A above. This polyvalent antiserum has been absorbed for the removal of cross reactions between serotypes listed in group A. Esch. coli antiserum polyvalent group B is a mixture of the Esch. coli serotypes listed in group B.

Bacteriological Methods

Fecal specimens were streaked on three mediums, blood agar, eosin-methylene blue agar, and MacConkey's agar plates. After incubation for 16 to 20 hours cultures were examined for colonies typical of Esch. coli. The colonies were characterized as gray, nearly flat, nonhemolytic, smooth, and opaque. Often portions of individual colonies that appeared on the blood agar plates were directly tested with polyvalent antiserums. If a strongly positive result of the slide agglutination test was obtained by this procedure, it was considered presumptive evidence that one of the particular Esch. coli serotypes was present in the specimen. Also, five or more colonies were tested by this procedure to determine the percentage of colonies that reacted in the antiserum. Positive agglutinating Esch. coli colonies were transferred to nutrient agar slants. The slants were inoculated over the entire surface in order to obtain maximum growth. After incubation these slants were used for biochemical and serologic studies. Some of the growth from the agar slant culture was emulsified in about 0.5 ml. of isotonic sodium chloride solution. Droplets of this heavy suspension were tested for agglutination on slides with droplets of OB antiserums diluted 1:3. When living suspensions of freshly isolated strains of Esch. coli serotypes were tested in OB antiserums, agglutination in a specific antiserum occurred rapidly and usually was complete. When the bacteria under examination were agglutinated by one of the antiserums, the suspensions then were heated at 100 C for one hour, cooled, and retested in the same antiserum. The later tests were used for presumptive identification of the O antigens of the culture. In case positive slide reactions were obtained in one of the cultures with the heated suspensions, a confirmatory test for an O antigen was performed by the tube dilution method.

TABLE 2.—*Summary of Biochemical Reactions of Six Strains of Esch. Coli 0111:B_4, Two Strains of Esch. Coli 0127:B_8, and Two Strains of Esch. Coli 0125:B_{15} Isolated from Household Pets*

Strains	1	2	3	4-6	1	2	1, 2
Serotypes	0111.B_4	0111:B_4	0111:B_4	0111:B_4	0127:B_8	0127:B_8	0125:B_{15}
Reaction, Type							
Adonitol	—	—	—	—	—	—	—
Dulcitol	+	+	+	+	+	+	+
Sorbitol	+	+	+	+	+	+	+
Arabinose	+	+	+	+	+	+	+
Xylose	+	+	+	+	+	+	+
Rhamnose	+	+*	—	—	+*	+*	—
Maltose	+	+	+	+	+	+*	+
Salicin	+	+	+	+	+	+	+
Inositol	—	—	—	—	—	—	—
Lactose	+	+	+	+	+	+	+
Sucrose	+	+	—	+	+	—	—
Sorbose	—	—	—	—	—	—	—
Mannitol	+	+	+	+	+	+	+
Glucose	+	+	+	+	+	+	+
Indole	+	+	+	+	+	+	+
H_2S	—	—	—	—	—	—	—
Gelatin	—	—	—	—	—	—	—
Ammonium citrate	—	—	—	—	—	—	—
Potassium nitrate	+	+	+	+	+	+	+
Voges-Proskauer	—	—	—	—	—	—	—
Methyl red	+	+	+	+	+	+	+
Urea	—	—	—	—	—	—	—

* Delayed reaction.

Various organisms belonging in the family Enterobacteriaceae, including several nonenteropathogenic types of Esch. coli, possess O antigens which exhibit a remarkable similarity to those of enteropathogenic Esch coli. Since some of the antigens are almost identical it is possible, when using a concentrated antiserum, to cause the nonenteropathogenic organisms to be agglutinated. The fact that such a situation does exist necessitates a confirmatory test to eliminate the possibility of an improper diagnosis. The problem of heterologous O agglutinations can be easily remedied by diluting the serum as in the tube agglutination method. The suspensions were diluted and tested in serial dilutions of 1:60 to 1:1,920.

These enteropathogenic Esch. coli cultures were also subjected to a battery of carbohydrate and IMViC reactions. These organisms were found to be positive for indole and methyl red but negative for the Voges-Proskauer reaction. Urea was not produced. A detailed analysis of the biochemical behavior of these organisms is shown in tables 1, 2, and 3. All enteropathogenic Esch. coli types isolated produced acid and gas from glucose and lactose promptly within 24 to 48 hours. Some strains fermented sucrose and salicin and others did not.

Table 3.—*Summary of Biochemical Reactions of Thirteen Strains of Esch. Coli 055:B_5 Isolated from Household Pets*

Strains	1	2	3	4	5	6	7	8	9-13
Serotypes	055 B_5	055 B_5	055 B_5	055 B_5	055 B_5	055 B_5	055 B_5	055 B_5	055 B_5
Reaction, Type									
Adonitol	—	—	—	—	—	—	—	—	—
Dulcitol	+	+	+*	+	+*	+	+*	+	+
Sorbitol	+	+	+	+	+	+	+*	+	+
Arabinose	+	+	+	+	+	+	+	+	+
Xylose	+	+	+	+	+	+	+	+	+
Rhamnose	+	+	+	+	+	+	+	+	+
Maltose	+	+	+	+	+	+	+	+	+
Salicin	+	+	—	+	+	+	—	+	+
Inositol	—	—	—	—	—	—	—	—	—
Lactose	+	+	+	+	+	+	+	+	+
Sucrose	+	+	+	—	+	+	+	+	+
Sorbose	—	—	+	—	—	—	+	—	—
Mannitol	+	+	+	+	+	+	+	+	+
Glucose	+	+	+	+	+	+	+	+	+
Indole	+	+	+	+	+	+	+	+	+
H_2S	—	—	—	—	—	—	—	—	—
Gelatin	—	—	—	—	—	—	—	—	—
Ammonium citrate	—	—	—	—	—	—	—	—	—
Potassium nitrate	+	+	+	+	+	+	+	+	+
Voges-Proskauer ..	—	—	—	—	—	—	—	—	—
Methyl red ...	+	+	+	+	+	+	+	+	+
Urea	—	—	—	—	—	—	—	—	—

* Delayed reaction.

Occasional strains otherwise typical grew on Simmons citrate medium after four or five days of incubation.

Comment on Results

During the course of this study a number of enteropathogenic Esch. coli were isolated from 321 household pets, 237 dogs and 84 cats, who were apparently healthy. These symptomless excretors may have had extremely mild and transient diarrheas that were overlooked by their owners. Since enteropathogenic Esch. coli is primarily pathogenic in infants and children under 2 years of age, it is possible that the age of the animals may be an important factor in producing symptoms.

Some of the fecal specimens contained almost pure cultures of Esch. coli serotypes, while others were of mixed organisms. Twelve and one-half per cent of these pets harbored these organisms (tables 4 and 5). Of 41 strains of Esch. coli serotypes isolated from these pets 83% were from dogs and 17% from cats. Only one animal carried two types, 0111:B_4 and 0125:B_{15}. Esch. coli 026:B_6 strain predominated. A number of household pets from the same families were also examined, and it was found that almost all pets owned by a family carried the same organism (table 6). Direct and indirect contact of these pets with each other in an environment common to both points to the mode of infection with this group of serotypes. Only one family had both a dog and a cat. Esch. coli 0111:B_4 and 0125:B_{15} were isolated from the dog but the cat excreted only 0111:B_4.

Table 4.—*Distribution of Esch. Coli Serotypes in 321 Fecal Specimens from Household Pets*

		Serotypes						
Animals	Animals Tested, No	0111 B_4	055 B_5	026 B_6	0127 B_8	0125 B_{15}	Serotypes Isolated, No.	% Positive
Dogs ...	237	5	10	15	2	2	34	14
Cats	84	1	3	3	...	...	7	8
Total .	321	6(1 3%)	13(4.1%)	18(5.6%)	2(0.6%)	2(0.6%)	41	12.5

Seasonal Variation.—A higher percentage of positive cultures was obtained during the summer months. It has been demonstrated by previous workers that most of the human outbreaks in nurses and patients reported to pediatricians occurred during and at the end of the summer season. Therefore, it would seem logical that a higher percentage of these carriers in a community is directly propro-tionate to the number of outbreaks (see figure).

Epidemiology.—During the course of this study an 11-month-old baby was brought into the hospital with diarrheal manifestations of gastroenteritis due to enteropathogenic Esch. coli. The baby had some dehydration, acidosis, and a slight rise in temperature. On bacteriological examination of the stool Esch. coli 055:B_5 was isolated in pure culture and an antibiotic sensitivity test showed that the organism was highly sensitive to chloramphenicol, furazolidone, and neomycin sulfate. Chloramphenicol was given to the baby for seven days. Within 36 hours of starting therapy the baby was alert, hungry, and active, but stool culture continued to be positive for four days, although not in pure culture of the offending organism. After the fourth day of treatment with chloramphenicol neomycin sulfate was added to the medication. The patient was discharged after disappearance of the organisms from the stool. There was no clinical relapse in this case.

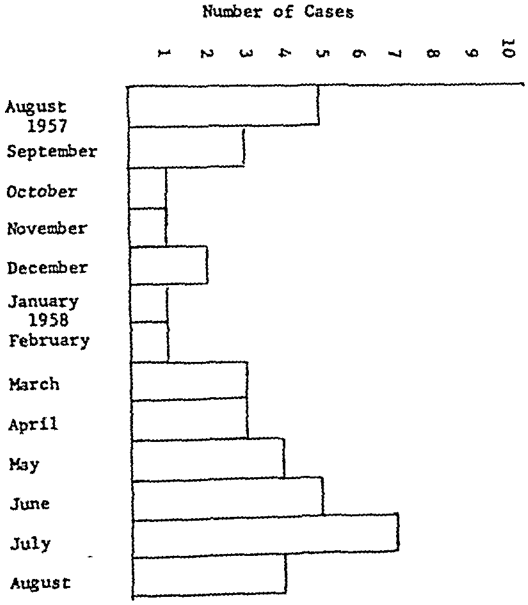
Table 5.—*Percentage Distribution of Esch. Coli Serotype Strains Isolated from 237 Dogs and 84 Cats of All Ages*

		Strains Isolated from Dogs		Strains Isolated from Cats	
Serotype	Strains Isolated, No.	No.	%	No.	%
0111:B_4	6	5	2.1	1	1.2
055 :B_5	13	10	4.2	3	3.6
026 :B_6	18	15	6.3	3	3.6
0127:B_8	2	2	0.8	...	...
0125:B_{15}	2	2	0.8	...	...
Total	41	34	83	7	17

During this time the father, mother, and a sibling aged 5 were examined and enteropathogenic Esch. coli was not found in their stools. The family had a dog. A rectal swab from this pet was examined and

Esch. coli 055:B_5 in almost pure culture was isolated. The dog had no history of any apparently abnormal condition for the last six months. In order to establish a relation between Esch. coli 055:B_5 isolated from the dog and that isolated from the baby, the presence of specific agglutinins was studied. It was found that baby's serum agglutinated heated suspensions of Esch. coli 055:B_5, dog strain, to a titer of 1:960. Efforts to determine the habits and environment of this pet which might tend to favor human infection were made. On questioning the parents it was found that the baby used to play in the living room on the carpet with the dog. The carpet was contaminated by the dog and the infection was carried by a hand-to-mouth pattern. One of the most outstanding features of this organism is its high degree of transmissibility, which is in direct contrast to other bacterial enteric diseases.

It is presumed that, in hospital outbreaks, the infection is brought into the nurseries by an infected mother or nurse who has had contact with some pets and is passed on to the babies. Good evidence has been presented by previous workers that enteropathogenic Esch. coli are spread from person to person by both direct and indirect contact. The disease has also been proved by previous workers to be air-borne. In their studies cross infection in the hospitals was found with excessive movement in changing diapers or carrying babies from one place to another, both of which released a significant number of organisms in the air. It was also demonstrated that the organisms could be found in large numbers on the floor mops used in contaminated cubicles and that the dust contained the organisms in viable form for 11 days. Furthermore, it has been shown in the experiments described by Hutchison that serotypes can remain viable in floor dust for as long as two weeks but that survival under shaded conditions is longer than in direct sunlight.



Seasonal variation in incidence of Esch. coli serotypes among 321 household pets examined from August, 1957, through August, 1958.

Although the majority of cases of infantile diarrhea occur in hospitals or other institutions, we know today that such infections occur also outside the hospitals. The carrier status of household pets leads us to the source of infection in human dwellings. It would seem probable that certain types of Esch. coli may give rise at times to an epidemic form of the disease and others to localized outbreaks or even sporadic cases. This close relationship of animal and human strains has a strong significance in the epidemiology of the disease. Obviously the importance of these organisms isolated from household pets in outbreaks of diarrhea in newborn infants is of the utmost importance, and an awareness of this fact should be present in public health, pediatricians', and hospital laboratories.

TABLE 6.—*Incidence of Esch. Coli Serotypes in Pets of Eight Households*

Pets Present in the Household, No.		Serotypes Isolated from Pets	
Dogs	Cats	Dogs	Cats
1	1	055:B_5	055:B_5
2	...	026:B_6	...
1	1	026:B_6	026:B_6
...	2	...	026:B_6
...	2	...	055:B_5
1	1	055:B_5	055:B_5
1	1	0111:B_4 0125:B_{15}	0111:B_4
2	...	055:B_5	...

Summary

A bacteriological investigation of enteropathogenic Escherichia coli in 321 household pets was carried out for a period of one year. Specific serotypes and biotypes of enteropathogenic Esch. coli 0111:B_4, 055:B_5, 026:B_6, 0127:B_8, and 0125:B_{15} were isolated from 237 dogs and 84 cats. Of these household pets 12.5% were found to be carriers of serotypes, and the incidence was higher during the summer months. There is a seasonal variation in the incidence of these serotypes among household pets, related to infantile diarrhea.

Dr. William W. Ferguson, Michigan Department of Health, and Dr. Pearl L. Kendrick, School of Public Health, University of Michigan, confirmed the identification of the cultures; the late Dr. Aaron Edwards supplied clinical information.

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CHROMOBLASTOMYCOSIS TREATED WITH LOCAL INFILTRATION OF AMPHOTERICIN B SOLUTION

REPORT OF SECOND CASE

Charles P. DeFeo, M.D.
and
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Chromoblastomycosis is a fungus disease which has been recognized in most of the tropical and semitropical countries of the world. To date 27 cases have been reported in North America, predominantly from the southern portion of the United States.[1] With the possible exception of those cases where wide surgical excision was curative and not disabling, attempts to find a successful therapy have not been encouraging.[2] The first successful treatment of a case of chromoblastomycosis by local infiltration of amphotericin B has been reported.[3] Fourteen months of observation after this local therapy, there was still no clinical or laboratory evidence of a recurrence in the patient. This route of administration of amphotericin B was instituted because the intravenous therapeutic blood level of 40 mcg. per milliliter necessary to inhibit the growth of the causative organism far exceeds the maximum intravenous dose tolerated by human beings.[4]

Because of the relative safety and ease of administration of this form of therapy, it was considered worthwhile to report the findings of the second patient successfully treated with local infiltration of amphotericin B. It is realized that these two cases constitute too small a number of patients for significant conclusions to be reached. However, the remarkably low incidence of chromoblastomycosis in the New York area prevents the collection of a more comprehensive series. It is hoped that the following case report may encourage others to treat a sufficiently large number of patients so that valid generalizations regarding the efficacy of this drug can be made.

Report of a Case

A 57-year-old Puerto Rican farm laborer was admitted to Bellevue Hospital with an ulcerative lesion on the dorsal surface of the right foot. The lesion had been present for 22 years and he associated its onset with his employment as a sugar cane cutter near San Juan, Puerto Rico. In 1936 he first noted a small, pea-sized, asymptomatic verrucoid nodule on the dorsal aspect of the right foot. The nodule slowly enlarged and was about 10 times its original size when the patient first sought medical attention. Numerous medicaments were applied topically; however, the lesion continued to enlarge. It reached such size by 1952 that amputation was advised. Although he refused radical surgery, he permitted local excision in 1953. The operative site never healed completely. The patient came to New York in 1955 and was unable to work because of pain in his foot. The lesion continued to enlarge up to the time of his admission to Bellevue Hospital in April, 1958, at which time he was unable to wear a shoe.

At physical examination a lesion 2 cm. in diameter was seen on the dorsal aspect of the right foot, immediately proximal to the second interphalangeal joint. It was indurated, slightly raised, crusted, and covered by a serosanguineous discharge. The second and third toes were erythematous, slightly edematous, and tender. This lesion was on the distal margin of an operative scar measuring 12 cm. in diameter.

A biopsy showed a granulomatous reaction in the cutis associated with pseudoepitheliomatous changes in the epidermis (fig. 2). Thick-walled, dark brown, spherical bodies about 10 to 15μ in

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From the Department of Dermatology and Syphilology, New York University Post-Graduate Medical School, and the Skin and Cancer Unit of University Hospital.

diameter were scattered in small groups throughout the cutis. Material obtained by curettage of the lesion showed numerous dark brown spores. Several of these spores were noted to be undergoing intracellular septation. The curetted tissue was placed on Sabouraud's agar and incubated at 20 C in order to culture the micro-organism. After one week a slightly raised, flattened, velvety, grayish-black, mouse-colored colony was observed. This slowly enlarged during the following three weeks. Microscopic examination showed the Hormodendrum type of sporulation. The mycological findings were those of H. pedrosoi.

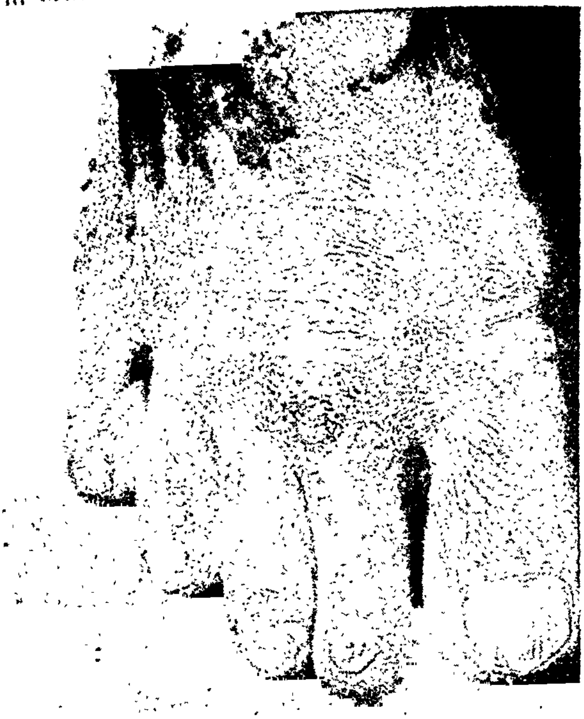

Fig. 1.—Dorsal aspect of right foot: ulcer measuring 2 cm. in diameter present at least 10 years before amphotericin B therapy was instituted on April 16, 1958.

A skin test was performed with an aqueous extract of the Hormodendrum culture obtained from our first patient.[3] Forty-eight hours after the intradermal injection of 0.1 cc. of this antigen, a 1.8-cm. circular area of erythema and edema appeared on the right forearm at the place of injection. A similar procedure was performed on several control volunteers who showed no reaction.

During the first five weeks of hospitalization the patient received no therapy other than bed rest. When, no evidence of healing was noted, after the five-week control period, treatment with amphotericin B was initiated. The concentration of amphotericin B solution used was 5 mg. dissolved in 1 cc. of a 2% procaine solution. Four weekly injections of 15 mg. (3 cc.) each were given directly into the lesion. A total of 60 mg. of amphotericin B was administered. The injections caused localized pain, slight elevation of temperature, and anorexia. No change in the blood urea nitrogen level was noted. The results of all routine hematological and urine studies were within normal limits. Repeated cultures after one month of therapy revealed no organisms other than Candida albicans, which was isolated on one occasion. Because of this finding, mycostatin ointment was applied topically for one week.

Three months after institution of amphotericin B therapy the area of ulceration had completely healed. The patient has been up and about for three months with no adverse effect. This is the first time the ulcer of his right foot has healed in five years. A biopsy specimen taken six months after therapy showed no evidence of any fungi, nor were any positive cultures obtained.

Summary

A case of chromoblastomycosis of 22 years' duration caused by Hormodendrum pedrosoi, with clinical cure of the patient, is the second case of favorable response to amphotericin B dissolved in 2% procaine solution and injected locally. Although the follow-up studies are of short duration, it is our opinion that this drug deserves further clinical trial.

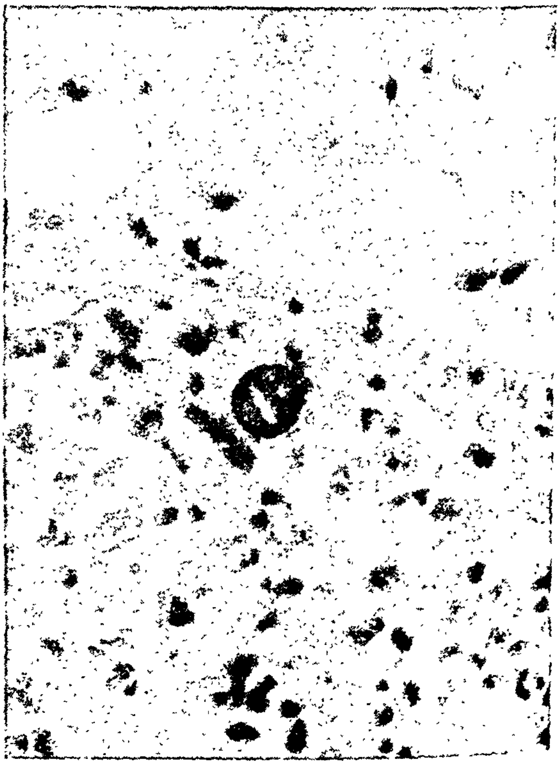

Fig. 2.—Skin biopsy specimen of right foot before therapy showing 10 μ spore of Hormodendrum pedrosoi undergoing intracellular septation. Surrounding tissue shows pseudoepitheliomatous hyperplasia and chronic inflammatory reaction.

140 E. 54th St. (22) (Dr. DeFeo).

The biopsy report was prepared by Dr. William Director and the mycological report by Dr. Emanuel Muskatblit.

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CLINICAL NOTES

STERILITY AFTER RADIOIODINE THERAPY FOR METASTATIC THYROID CARCINOMA

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and
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Radioiodine (I^{131}) has been used in the treatment of thyroid cancer metastases since 1943. The harmful radiation effects of this agent on the blood-forming organs are well recognized, but other body structures are seldom injured. Reports of permanent damage to the reproductive organs by I^{131} are exceedingly rare. The case we are reporting seems to represent a clear instance of injury to the testes from radioiodine administered as treatment for metastatic thyroid carcinoma.

Report of a Case

A 24-year-old man was found during the course of a routine x-ray examination of the chest in March, 1952, to have widespread diffuse nodular densities in both lung fields (fig. 1). He felt entirely well at this time, had lost no weight, and had no respiratory symptoms whatever. It was known that a roentgenogram of the chest in 1949 had shown no abnormalities. Physical examination was entirely negative except for a small firm lymph node present high in the left cervical chain and a slightly enlarged left thyroid lobe which was smooth and firm. Routine laboratory studies showed no deviant findings. Results of tuberculin, histoplasmin, and coccidioidin skin tests were negative. There were no abnormalities of his serum proteins. He had never been exposed to noxious dusts nor had he ever had any known pulmonary illness.

The cervical lymph node was excised and study of a frozen section proved it to contain metastases from carcinoma of the thyroid. The entire thyroid gland was removed and a radical neck dissection was performed on the left side. Most of the thyroid gland was found to be replaced by carcinoma. The lymphatic structures of the neck were diffusely invaded by the tumor. Microscopic study revealed the lesion to be a mixed adenocarcinoma of the thyroid with a predominantly papillary pattern (fig. 2).

It was concluded that the lung lesions were metastases from the thyroid carcinoma. Dr. Rulon Rawson of the Memorial Hospital for Cancer and Allied Diseases, New York City, studied and treated the patient in July, 1952, and administered 246 mc. of I^{131}. In February, 1953, an additional 317 mc. of radioiodine was given. In each instance the patient was pretreated with thiouracil. Myxedema developed after the second dose of I^{131}, and in July, 1953, the patient was placed on replacement therapy with triiodothyronine and he has continued this medication until the time of writing.

The patient has remained quite well, except for some limitation of his respiratory reserve due to widespread pulmonary fibrosis secondary to radiation. There has been no additional evidence of tumor spread, and serial roentgenograms of the lungs have shown little or no change in the past six years. The cancer appears to be arrested and probably cured six years after treatment.

From the Department of Medicine, University of Oregon Medical School.

In January, 1956, three years after the last dose of I^{131}, the patient submitted himself for evaluation of his fertility. Repeated studies of his ejaculate failed to reveal the presence of sperm. This observation seemed most intriguing since he was previously known to be fertile and is the father of a child born in 1952. Biopsies were performed on specimens from both testes. Microscopic studies showed seminiferous tubules to be much reduced in size. Moderate fibrosis of the tunica propria was present, but little change in the basement membrane was noted. There was a complete lack of germ cells in the tubules and no evidence of spermatogenesis. The Sertoli and Leydig cells appeared normal. Sections from both testes showed similar findings (fig. 3). The patient's urine contained markedly increased amounts of pituitary gonadotropins, the titer being comparable to that of a castrated man. Urinary estrogen and 17-ketosteroid levels were within normal range for men.

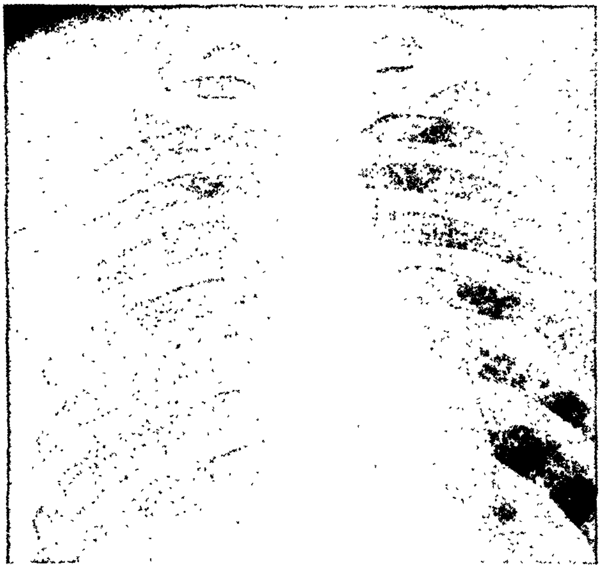

Fig. 1.—Roentgenogram of chest, prior to thyroidectomy and radioiodine therapy, showing widespread fine nodules of metastatic carcinoma.

Comment

We were able to find only one published clinical report of radiation injury to the male gonads after large doses of radioiodine. Duffy and co-workers[1] reported a 50-year-old man in whom metastatic thyroid carcinoma had been treated with I^{131} and in whom a testis biopsy later revealed atrophic changes and absence of spermatogenesis.

Radioiodine in large doses may disturb the menstrual cycle and produce transient amenorrhea. Maloof and co-workers[2] reported two instances in which menses failed to reappear after such treatment. In both these patients large osseous metastases were present in the pelvis, which were shown to concentrate I^{131}. One of the patients died after receiving 2,000 mc. of I^{131} over a five-year period, and an autopsy showed fibrosis and cortical atrophy of the ovaries.

Animal experiments designed to show the effects of an internally administered radioactive isotope demonstrate the testes to be quite vulnerable.[3] Such studies reveal a rapid and complete recovery if radiation injury is minimal, but recovery almost never occurs when all stages of spermatogenesis are interfered with. There seems little likelihood of recovery of tubular function in our patient since there was no indication whatsoever of spermatogenesis three years after the last dose of I^{131} was administered. That the absence of sperm was due to seminiferous tubule defect and not secondary to pituitary failure was demonstrated by the presence of abnormally large amounts of gonadotropin in the patient's urine. It is also noteworthy that the Leydig cells which appeared histologically normal were also functionally intact, as demonstrated by the normal amounts of estrogens and 17-ketosteroids in the patient's urine.

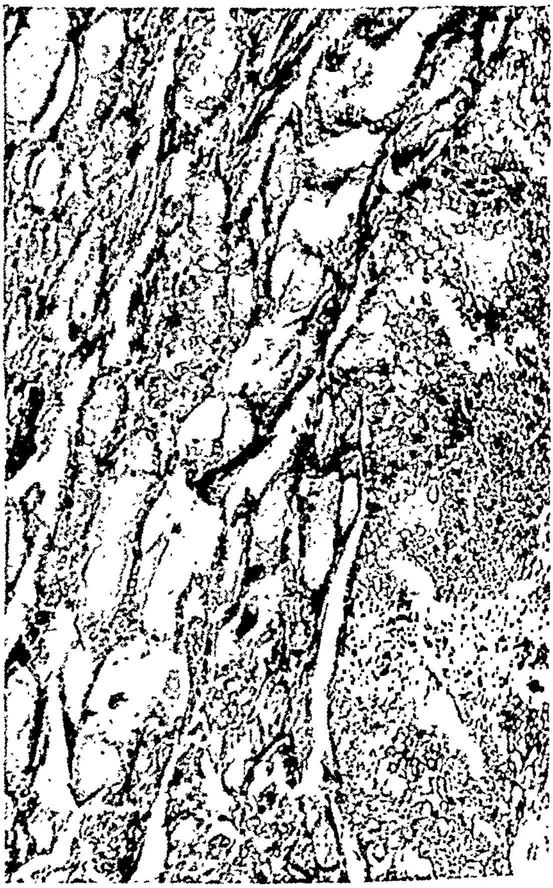

Fig. 2.—Photomicrograph of section from carcinomatous thyroid, showing predominantly papillary pattern (× 100).

Maloof,[2] in a follow-up study of patients treated with radioiodine, evaluated the function of the pituitary, adrenals, gonads, kidneys, liver, and hematopoietic system. There was surprisingly little harmful effect noted on the blood-forming organs. When such changes did occur they appeared as a transient decrease in the white blood cells, especially in the lymphocytic series. One fatal case of pancytopenia was described. One of us (H.K.) had a patient who received 125 mc. of I^{131} for treatment of skeletal metastases from a thyroid carcinoma. The patient developed fatal pancytopenia. Marrow biopsy revealed the presence of cancer cells. Myeloid leukemia occurred in 2 of 16 patients reported by Seidlin,[4] appearing four and five years, respectively, after administration of cancericidal doses of radioiodine. Hypochromic anemia resistant to oral iron therapy has been noted. According to Rall and co-workers[5] tracer studies with use of radioactively tagged iron demonstrated that the red blood cells in such patients do not use iron in a normal manner.

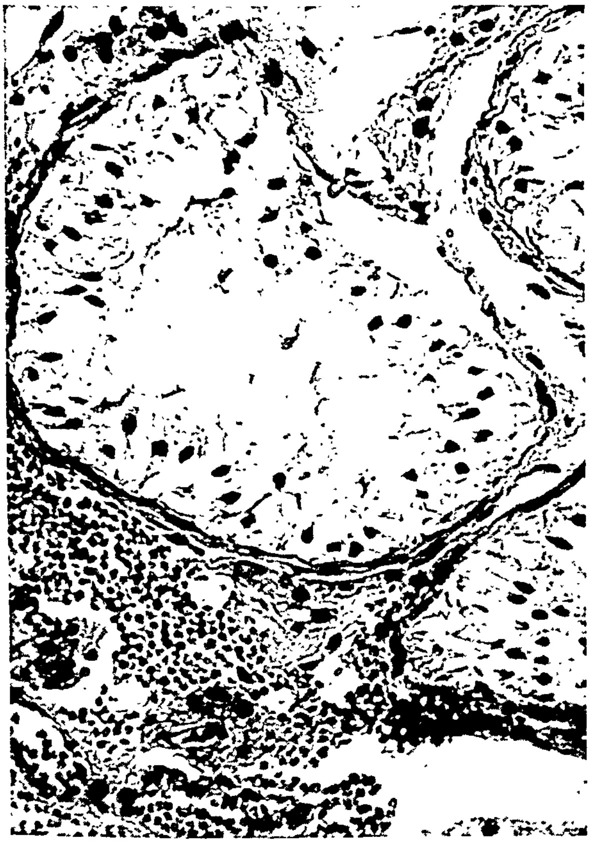

Fig. 3.—Photomicrograph of biopsy specimen from testis, showing reduction in size of seminiferous tubules, some fibrosis of tunica propria, absent germ cells, no evidence of spermatogenesis, and normal Sertoli and Leydig cells (× 320).

Radiation pneumonitis and fibrosis leading to varying degrees of pulmonary insufficiency have been reported in several patients receiving radioiodine for the treatment of extensive pulmonary metastases.[6] In a few instances these changes were severe enough to cause death. The patient herein reported had considerable exertional dyspnea for many months after his second dose of radioiodine, due to widespread pulmonary fibrosis. These changes are abundantly manifested in his lungs at the present time, although he tolerates mild exertion with minimal dyspnea. His vital capacity is 1,600 cc. (41% of the predicted normal value) and the one-second vital capacity is 1,500 cc.

Our patient received medication with several drugs at various times, in addition to the treatment with radioiodine. Large doses of thiouracil were used as pretreatment for an extended period prior to each dose of radioiodine. He has received triiodothyronine continuously in sufficient dosage to maintain his metabolic rate near normal. Methyltestosterone, 10 mg. daily, was given for several months during 1953. There is no evidence with which we are familiar that any of these agents produces testicular damage comparable to that described in this patient. The conclusion seems justified that radiation injury resulting from treatment with I^{131} is responsible for the patient's damaged testes.

Summary

A 24-year-old man became sterile after he received 563 mc. of I^{131} for pulmonary metastases from thyroid carcinoma. Testicular biopsies revealed histopathological changes consistent with a diagnosis of radiation injury, and we believe that these changes are responsible for his sterility. Prior to the radiation therapy the patient was known to be fertile. Results of hormone assays were compatible with the histological changes noted in the testes. It is possible that long-term follow-up study of patients similarly treated will reveal more examples of radiation injury to the male gonads.

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Dr. Warren O. Nelson of the Population Council, the Rockefeller Institute, reviewed the microscopic sections. Dr. William M. Laidlaw of the Endocrine Laboratory, University of Oregon Medical School, performed the hormone assays.

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GLYCOGEN METABOLISM

ONE of the major advances of medical science was the demonstration of in vitro synthesis of glycogen by purified phosphorylase. This discovery was the forerunner of an explosive increase in knowledge of the processes of biosynthesis. The rapid unfolding of the nature of enzymatic reactions has revolutionized biochemistry and is beginning to have a major impact on all aspects of biology and medicine.

Concepts of the enzymatic reactions responsible for the biosynthesis of polysaccharides have been completely changed in the past 10 years as a result of the discovery of uridine nucleotides. According to recent reports,[1] uridine diphosphate glucose is the key intermediate in the synthesis of glycogen. This nucleotide, originally discovered by Leloir[2] as the coenzyme involved in the interconversion of glucose and galactose, is composed of uracil, ribose, two phosphate groups, and glucose. The uridine portion of the molecule (uracil, ribose, and phosphate) is a component of ribonucleic acid. Like other nucleotides it serves a dual role, appearing as a component of ribonucleic acid and as a nucleotide to form a coenzyme involved in biosynthetic reactions.

The discovery that uridine diphosphate glucose participates in the synthesis of glycogen indicates a hitherto unsuspected pathway for the formation of glycogen from glucose-1-phosphate. Earlier investigations indicated that glycogen is formed by the following reaction:

$$(1)\ \text{glucose-1-PO}_4 + \underset{\text{phosphorylase}}{\rightleftharpoons} \text{glycogen} + \text{PO}_4$$

The more recent publications suggest that glycogen is formed as follows:

$$(2)\ \text{uridine-diphosphate glucose} \rightleftharpoons \text{glycogen} + \text{uridine diphosphate.}$$

Reaction 1 has an equilibrium which is displaced to the left, i. e., the breakdown of glycogen is favored. This is particularly true within the cell, since intracellular fluid contains a relatively high concentration of phosphate. The second reaction is displaced toward the right, i. e., glycogen synthesis is favored.

Uridine diphosphate glucose is formed from glucose-1-phosphate by the following reaction:

$$(3)\ \text{glucose-1-phosphate} + \text{uridine triphosphate} \rightleftharpoons \text{uridine diphosphate-glucose} + \text{pyrophosphate.}$$

Uridine triphosphate may be reformed from uridine disphosphate by the following reaction:

$$(4)\ \text{uridine diphosphate} + \text{adenosine triphosphate} \rightleftharpoons \text{uridine triphosphate} + \text{adenosine diphosphate}$$

The net result of reactions 3 and 4 permits the use of energy supplied by adenosine triphosphate for the synthesis of glycogen.

It thus appears that both reactions 1 and 2 represent pathways for the formation of glycogen from [illegible] However, the difference be- [illegible] of the two reactions suggests that reaction 1 may be a more suitable pathway for the breakdown of glycogen while reaction 2 may be more suitable for glycogen synthesis. Since both epinephrine and glucagon have been shown to be involved in the activation of phosphorylase, the enzyme catalyzing reaction 1, the ability of these two hormones to make glucose available may be explained by this reaction.

The mechanism of synthesis of a large number of disaccharides and polysaccharides is similar to reaction 2.

Numerous recent studies indicate that uridine diphosphate glucose is typical of a large family of uridine nucleotides which contain a variety of different sugar moieties. The glucose may be substituted by uronic acids, N-acetylated hexosamines, pentoses, or other monosaccharides. The appropriate nucleotides serve as donors of monosaccharide units by a series of reactions typified by equation 2. Already synthesis of sucrose, lactose, trehalose, cellulose, and hyaluronic acid have been shown to proceed by this mechanism. That this mechanism represents the general pathway by which monosaccharides are transferred in nature seems likely. Many new examples of such reactions can be anticipated in the near future.

The discovery of the role of uridine diphosphate glucose in glycogen synthesis opens new avenues for the study of carbohydrate metabolism. It seems likely that unexplained phenomena related to disturbances in human carbohydrate metabolism may find explanation as disturbances of this new pathway. The possible role of hormones in regulating the rate of these enzymatic reactions needs elucidation. New developments in this area may be confidently expected as a result of this important advance.

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[1] Leloir, L. F., and Cardini, C. E.: Biosynthesis of Glycogen from Uridine Diphosphate Glucose, J. Am. Chem. Soc. 79:6340, 1957. Villar-Palasi, N. C., and Larner, J.: Uridine Coenzyme-linked Pathway of Glycogen Synthesis in Muscle, Biochim. Biophys. Acta 30:449, 1958. Robbins, P. W.; Traut, R. R.; and Lipmann, F.: Glycogen Synthesis from Glucose, Glucose-6-phosphate, and Uridine Diphosphate Glucose in Muscle Preparations, Proc. Nat. Acad. Sc. 45:6, 1959.

[2] Leloir, L. F.: Enzymatic Transformation of Uridine Diphosphate Glucose into Galactose Derivative, Arch. Biochem. Biophys. 33:186-190 (Sept.) 1951.

COUNCIL ON NATIONAL DEFENSE

INDIVIDUAL SURVIVAL TRAINING

Banning G. Lary, M.D.
and
Julian Rickles, M.D., Miami, Fla.

With the ability of an enemy to deliver thermonuclear destruction on this nation, and because it has been estimated 50 million casualties would follow an all-out attack, it is mandatory that each person educate himself in survival techniques. To provide a shelter program, all states have now enacted civil defense legislation. However, individual survival education of the citizens is a function of local government and is entirely voluntary on the part of the citizens.

Civil defense personnel have developed various educational programs for the citizenry. In Dade County, Florida, only a minority of the public volunteer students finished these courses. It was felt a shorter fact-filled course would be better received. This course was to stress the prevention of death by prompt simple treatment. Through cooperation of the Dade County Medical Association with the Dade County Civil Defense organization, a program entitled, "Individual Survival Training" evolved.

This program was divided into three two-hour weekly lectures given by physicians and paramedical personnel. The first lecture consisted of an introduction to the basic concepts and the destructive potential of atomic and thermonuclear weapons. In addition, simple survival techniques were briefly discussed. Emphasis was placed on the storage of foods, the necessity for stockpiling a battery radio with which to receive Conelrad instructions, and the most effective types of shelter. The second portion of the first lecture consisted of a discussion of respiratory obstructions and injuries. The second lecture discussed the treatment of the various types of lacerations and shock. Attention in the third lesson was directed to the treatment of fractures, burns, and artificial resuscitation.

It was found the greatest number of people could be reached in the evening between the hours of 8 and 10 p. m. Physician training for the lectures consisted of briefings at which fundamentals of emergency care were reiterated. Physicians were encouraged to attend the civil defense programs offered by the armed services, and their expenses were partially defrayed from local civil defense budgets.

While the audiences were told that many of the treatments recommended would be applicable in daily living, it was nevertheless stressed that atomic catastrophe-concepts necessitated short cuts from normally accepted treatments. It was pointed out that, with the knowledge obtained from the lectures, the audience could initiate "self-care" and "buddy-care" of a degree which would approximate that which a physician could render under catastrophic circumstances. It is believed that audience participation in the question-answer technique was one of the most important steps used to clarify the material and that people were genuinely interested in learning survival techniques. Community knowledge of the program far exceeded the attendance. This was made possible by the cooperation of the full-time and volunteer civil defense personnel, the P. T. A., and the press.

MEDICAL FILM REVIEWS

NEW FILM ADDED TO A. M. A. MOTION PICTURE LIBRARY

Congestive Heart Failure: 16 mm., color, sound, showing time 10 minutes. Cleared for television. Technical Advisor: William D. Stroud, M.D., Philadelphia. Produced by Transfilm Incorporated for Merck Sharp and Dohme. Procurable on loan (service charge $1.00) from Motion Picture Library, American Medical Association, 535 N. Dearborn St. Chicago 10.

By limited animation, this film first shows how the normal heart functions and then explains how a weakened heart reacts when excessive demands are made on it. High blood pressure, pregnancy, anemia, or respiratory infections put demands on the heart which cause already weakened muscle fibers to stretch and thicken, and the heart grows larger in order to pump enough blood. Congestive heart failure develops when no further enlargement is possible and the heart fails to do its work. Also covered in the film are specific remedial steps to improve the heart's efficiency, including the reducing of the body's demands on the heart and increasing the heart's ability to pump out blood. It emphasizes that with proper care, a patient with congestive heart failure has a good prospect of returning to a relatively normal life. This film is recommended for physicians who are called on to speak before high schools, parent teacher associations, and health education classes.

MEDICAL NEWS

ALASKA

Trudeau Society Organized.—The Alaska Trudeau Society was organized in Anchorage on Aug. 18. American Trudeau Society members residing in Alaska and other physicians interested in respiratory diseases attended this organizational meeting. The officers elected were: president, Dr. Francis J. Phillips, Anchorage; vice-president, Dr. Ernest W. Gentles, Bartlett; secretary-treasurer, Dr. Jose E. Silva, Anchorage. In addition to the officers, the following were elected to the executive committee: Dr. Jack W. Gibson, Juneau; Dr. John I. Weston, Fairbanks; and Dr. David L. Sparling, Mt. Edgecumbe.

ARIZONA

Physicians Meeting in Tucson.—The American College of Physicians Arizona regional meeting will be held Saturday, Dec. 12, at the El Conquistador Hotel, Tucson. The morning panel, "Lipids in Health and Disease," will be moderated by Dr. Leslie R. Kober, Phoenix. A discussion and question-and-answer period will follow the panel. The program includes the following papers:

Accumulated Experiences with the Artificial Kidney, Dr. Kenneth E. Johnson, Phoenix.
Systemic Lupus Erythematosus, Dr. Harry E. Thompson, Tucson.
Experimental Distention of the Human Gallbladder: Effect on the Electrocardiogram and Clinical Implications, Dr. Howard Wakefield, Chicago.
Cardiac Tumors, Dr. Meyer Markovitz, Phoenix.
Myelofibrosis, Dr. Preston J. Taylor, Tucson.
Extrapulmonary Coccidiodomycosis, Dr. Charles A. Janda, Tucson.
Tissue Culture, Dr. Charles A. L. Stephens Jr., Tucson.

At the banquet (7:30 p. m.) Dr. Howard Wakefield, Chicago, regent of the college, will present "Some Activities of the American College of Physicians."

CALIFORNIA

Radiology Meeting in Los Angeles.—The 12th annual Midwinter Radiological Conference, sponsored by the Los Angeles Radiological Society, will be held at the Statler Hotel, Los Angeles, Jan. 30-31. Guest speakers will be Dr. John A. Evans, New York City; Prof. Knut Lindblom, Stockholm, Sweden; Dr. James J. Nickson, New York City; and Dr. Ernest Rohan Williams, London, England. The conference fee of $20 includes two luncheon meetings featuring questions and answers. A banquet ($7.50 per plate) will be held Jan. 30. Reservations may be made through Dr. Sidney D. Zucherman, 3741 Stocker St., Los Angeles 8. Courtesy cards will be available to residents in radiology and radiologists in the Armed Forces by advance registration, with reduced tariff for the luncheons and banquet.

Society News.—At the last meeting of the California State Board of Medical Examiners held in Sacramento, the following officers were elected for 1959-1960: Dr. Leo J. Adelstein, Los Angeles, president; Dr. George S. Johnson, San Francisco, vice-president; and Dr. Louis E. Jones, Roseville, secretary-treasurer.——The Los Angeles Obstetrical and Gynecological Society, Inc., recently established a permanent office for the society at 5478 Wilshire Boulevard, Room 222, Los Angeles 36 (WEbster 4-1551). Officers for 1959-1960 are: president, Dr. Dan Golenternek, Beverly Hills; vice-president, Dr. John L. Gaspar; and secretary-treasurer, Dr. Leon J. Shulman. Meetings are held on the second Tuesday in September, November, January, March, and May.——The 1959-1960 officers of the Los Angeles Radiological Society elected in June who took office in September are: president, Dr. Putnam C. Kennedy, Glendale; vice-president, Dr. Robert E. Rickenberg, Los Angeles; treasurer, Dr. Robert B. Engle, Pasadena; secretary, Dr. Denis C. Adler, Los Angeles. The society meets the second Wednesday of September, November, March, April, and June, at the Los Angeles County Medical Association Building.——The Los Angeles County Heart Association has announced that its new headquarters for Los Angeles county are at 2405 W. Eighth St. (corner of Eighth and Parkview), Los Angeles 52 (DUnkirk 5-4231). The headquarters were formerly located at 660 S. Western Ave.

COLORADO

Conference on Prematurity.—Authorities from the 18 premature infant centers in the U. S. and Hawaii met for a Conference of Premature Infant Center Directors and Obstetricians Nov. 9-10 in Denver. Main purpose of the conference was a polling of knowledge as to the cause of prematurity and its prevention. The conference was supported by a grant from the U. S. Children's Bureau, and was also sponsored by the Colorado State Health Department and the University of Colorado School of Medicine. The program included a panel discussion Nov. 9 on the causes of respiratory distress and other ills of the newborn, and an afternoon review

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

of surgical technique of cervical surgery. The scientific program Nov. 10 included a review of research programs at the various centers.

FLORIDA

Society News.—The Florida West Coast Radiology Society elected the following officers for the coming year: Dr. Charles M. Gray, Tampa, president; Dr. James T. Shelden, Lakeland, vice-president; and Dr. Joseph C. Rush, St. Petersburg, secretary-treasurer. The society meets quarterly at the Tampa Terrace Hotel.——At the 27th annual meeting of the Florida Radiological Society the new officers for 1959-1960 were elected as follows: president, Dr. Russell D. D. Hoover, West Palm Beach; president-elect, Dr. John S. Stewart, Fort Myers; vice-president, Dr. Alfred G. Levin, Miami; treasurer, Dr. Ivan Isaacs, Jacksonville; and secretary, Dr. John P. Ferrell, 166 4th Ave., St. Petersburg.

GEORGIA

Personal.—Dr. Winston E. Burdine, Atlanta, National Commander of AMVETS, accepted an appointment as chairman of the advisory board of the American Association of Doctors' Nurses, according to an announcement by Mr. Bob Bickford, executive director of the association, a nonprofit organization whose purpose is "to bring recognition to the nurse who works in a doctor's office."——Dr. John M. Wilkins, St. Mary's Hospital, Athens, was elected secretary of the Crawford W. Long Medical Society.

ILLINOIS

Report on Deaths from Malignant Neoplasms.—The State of Illinois Department of Public Health released a statistical summary on Illinois residents, through the year 1957, entitled "Malignant Neoplasm Deaths." Total deaths from cancer among Illinois residents indicate a continuing increase, with 14,500 reported in 1950 and 16,333 reported in 1957. Although there were 14,379 deaths reported in 1949 indicating the stomach as the site with highest incidence (1,706), figures for 1957 show a decrease in deaths for stomach cancer (1,505). The highest incidence of cancer with regard to site for 1957 was that of the large intestine (except rectum) with 1,894 deaths and the second and third were the stomach and the breast (1,470). The number of deaths from leukemia was 709 in 1957 compared with 376 in 1941, with the highest number of cases in the 70-79 age group (152 cases). Deaths from cancer of the lung for 1957 numbered 2,019, which represents a continuing increase for each year from 1941, when 639 were reported. The largest percentage of distribution for 1957 for deaths from cancer of the lung, trachea, bronchus, and pleura, was 37.2% for the 60-69 age group.

Chicago

Surgeons Present Lecture Series.—The fourth series of lectures of the International College of Surgeons Hall of Fame and the School of the History of Surgery and Related Sciences at the Hall of Fame began Oct. 20 with Dr. Leon Unger, associate professor of internal medicine and allergic diseases, Northwestern University, presenting "The History of Allergy." On Nov. 24 Dr. Walter C. Alvarez, professor emeritus of the University of Minnesota, Minneapolis, presented "The History of Gastroenterology." Subsequent lectures are as follows:

Jan. 12—The Physician as a Book Collector—Notes on Famous Libraries, Mr. Herman Henkle.
Feb. 2—Highlights of Orthopedic Surgery, Dr. Philip Lewin.
Feb. 23—The Bookplates of Physicians, Dr. Morris Fishbein.
March 15—The History of Blood Transfusion, Dr. Richard Lewisohn, New York City.
April 5—The History of Pulmonary Tuberculosis, Dr. Jerome R. Head Jr.
April 26—Nicholas Senn and the Medical Center of Chicago, Dr. Manuel E. Lichtenstein.
May 10—Architects of Chicago Medicine, Dr. Frederick Stenn.

Personal.—Dr. Frederick Steigmann, director of clinical investigation of the Hektoen Institute for Medical Research of Cook County Hospital, invited to the Argentinian Gastroenterology Congress in Cordoba (Aug. 16-21), also presented papers before gastroenterological groups in Caracas (Venezuela), Rio de Janeiro (Brazil), Buenos Aires (Argentina), Lima (Peru), and Tegucigalpa (Honduras). He was given honorary membership in the Argentinian Gastroenterological Association, the Society of Internal Medicine and the Pathological Society of Buenos Aires, and the Gastroenterological Society of Peru.——Dr. James J. Callahan, chairman of bone and joint surgery at Loyola University's Stritch School of Medicine, was named chairman of the new Loyola Medical Loyalty Fund. Dr. Callahan served as co-chairman of a 20-man medical school planning committee which recommended the construction of a multi-million dollar medical center on 54 acres in northwest Chicago on the Skokie (Ill.) border.

KANSAS

Accidental Farm Deaths in 1959.—The Division of Vital Statistics of the Kansas State Board of Health has issued its 29th annual Agricultural Accidental Death Report. The tractor is still the greatest cause of farm work accidental deaths in Kansas, as it has been for a number of years. The 16 deaths caused by tractor accidents last year were five fewer than the 1957 toll. The total of 43 persons who were fatally injured while doing farm work in 1958 is a drop from 50 killed in 1957, and equals the previous low record of such deaths in 1956. Burns caused seven deaths, more than in any year since 1945. There were six deaths due to falls, and six to farm machinery other than tractors; three were caused by vehicular accidents, and one each by suffocation, lightning, drowning, firearms, and animal injury. In the last 10 years, persons in age groups past 60 years suffered the most fatal injuries while engaged in farming activities, with 42% of the total. Agriculture ranks first, in terms of on-the-job accident fatalities in Kansas, with 39% of the total occupational deaths from 1954-1958 inclusive. However, agriculture is the major Kansas industry, using nearly one out of every five employed persons.

MARYLAND

Foreign Lecturer.—Mr. W. Stanley Walton, professor of public health, The London School of Hygiene and Tropical Medicine, London, England, presented "The Thousand Family Survey in Newcastle Upon Tyne" as a public lecture, at the School of Hygiene and Public Health, Johns Hopkins University, Baltimore, on Nov. 20.

MASSACHUSETTS

Dr. Stanier Gives Annual Lecture.—The third annual J. Howard Mueller Memorial Lecture, honoring the late head of the department of bacteriology and immunology at the Harvard Medical School, was given by Roger Stanier, Ph.D., of the University of California at Berkeley. His subject was "Bacterial Photosynthesis." Dr. Mueller, whom the lecture honors, was, at the time of his death in 1954, a Charles Wilder Professor of Bacteriology and Immunology at Harvard.

Dr. O'Brien Receives Radiology Award.—The Gold Medal of the Radiological Society of North America was presented Nov. 19 to Dr. Frederick W. O'Brien, of Boston. The presentation ceremony took place during the 45th annual meeting of the society in Chicago. The medal was presented by Dr. Laurence L. Robbins, Boston, president of the society and director of radiology at the Massachusetts General Hospital. Dr. O'Brien is past-president of the American Radium Society and in 1947 became president of the Radiological Society of North America. He is emeritus professor of radiology of Tufts University Medical School, his alma mater. Dr. O'Brien continues his activities as a trustee of the American Board of Radiology.

Grant for Research Building.—A matching grant of $1,369,460 by the United States Department of Health, Education, and Welfare was awarded to the Harvard School of Public Health for the first stage in the construction of a nine-story research building. The new building will be erected adjacent to an existing structure housing a portion of the school's research activities at the southeast corner of Huntington Avenue and Shattuck Street in Boston. The proposed research building will be of brick, concrete and steel construction, and will house laboratories for research in environmental health and nutrition. About 38,000 square feet of space will be available for research, maintenance, and service activities. Construction is expected to start in mid-1960. The first portion will include a sub-basement and basement to house the engineering activities of the school's recently created division of environmental hygiene. The first four floors above the ground will be concerned with the division's research relative to the effect of radioactive fallout and air pollution. A portion of this space is being planned to house the school's research program in aviation health and safety, space biology, and highway safety. Research activities of the school's department of nutrition will be placed in the upper four floors of the new building. A second phase of the building program, being studied, looks to the addition of four more floors for future growth and development of the school.

NEW JERSEY

Hospital Plans Expansion.—Riverside Hospital has announced expansion plans calling for the erection of a new wing designed to expand its facilities for the care of medical and surgical patients by 50%. Plans have been under way for some time for a Riverside Hospital Expansion Fund drive to raise $110,000 to build and equip the new wing. Plans include a new maternity wing to house 12 beds and corresponding bassinets. The present maternity wing will be turned over to medical-surgical use and rearranged to accommodate 24 beds, of which 16 will be adult beds, including 4 single-room beds, and 8 will be beds for patients in pediatrics. The hospital's medical-surgical facilities will be increased by 50% and the number of available single-room beds by 100% by adding the proposed wing. Riverside Hospital became the fifth hospital in Morris County when it opened its doors to the public in November, 1955, as a nonsectarian community hospital.

NEW YORK

Symposium on Metabolism.—"Salt and Water Metabolism" will be the subject of a two-day symposium to be held by the New York Heart Association at the Hotel Biltmore, New York City, Dec. 11-12. Dr. Alfred P. Fishman, chairman of the association's Scientific Sessions Committee, is in charge of the program, and 23 speakers will take up all phases of the subject. Topics to be considered include Theory of Solutions; Intrarenal Sites of Salt and Water Exchange; Extrarenal Salt and Water Metabolism; and Extrarenal Regulation of Salt and Water Exchange. Dr. Karl J. Ullrich, University of Gottingen, Germany, will speak on "Functions of the Collecting Duct." An after-dinner address that evening will be given by George Wald, Ph.D., of Harvard University, Boston, entitled "Salt, Water and Vertebrate

Metamorphosis." Application for registration should be made to Dr. Alfred P. Fishman, % N. Y. Heart Association, 10 Columbus Circle, New York 19. No fee is involved.

Personal.—Dr. Francis O. Harbach, clinical professor of urology at the Upstate Medical Center, Syracuse, was elected president of the northeast section of the American Neurological Society. Dr. Harbach was secretary-treasurer of the organization from 1952-1958.——Dr. Selig H. Katz, Albany, was appointed an assistant director of the New York State Health Department's Bureau of Maternal and Child Health. Dr. Katz will be assistant director for Maternity and Newborn Services.

OHIO

Society News.—The following officers of the Ohio Society of Anesthesiologists were elected Sept. 19: president, Dr. John P. Garvin, Columbus; vice-president, Dr. DeForest W. Metcalf, Youngstown; and secretary-treasurer, Dr. Nicholas G. DePiero, Cleveland.——The annual election of the American Medical Women's Association of Cincinnati, Branch II, was held with the following officers elected: president, Dr. Ruth C. Ferris, Cincinnati 20; vice-president, Dr. Henrietta M. Miller, Cincinnati 8; treasurer, Dr. Eileen M. O'Ferrell, Cincinnati 11; and secretary, Dr. Mary M. Martin, 3035 Clifton Ave., Cincinnati 20.

PENNSYLVANIA

State Society Changes Name.—At the 109th annual session of the Medical Society of the State of Pennsylvania in Pittsburgh Oct. 18-23 the name of the organization was officially changed to the Pennsylvania Medical Society.

Society News.—At the June 10 meeting of the Pittsburgh Roentgen Society the following officers were elected for 1959-1960: president, Dr. Lewis E. Etter; vice-president, Dr. Theron B. Childs; secretary, Dr. Charles N. Chasler, Elizabeth Steel Magee Hospital, Pittsburgh 13; and treasurer, Dr. Julius W. Ambrose.

Philadelphia

Dr. Richards Receives Flexner Award.—Dr. Alfred N. Richards, emeritus professor of pharmacology and former vice-president for medical affairs at the University of Pennsylvania, received the Association of American Medical Colleges Abraham Flexner Award for "long and distinguished service to medical education" on Nov. 2. The award was established in 1958 in the name of the man who presented a report on the teaching of medicine in 1910 which led to a "revolution in medical education, forced the closing of many below-standard medical schools, and laid the basis of medical education as it is known today." Dr. Richards, 83, was chairman of the Committee on Medical Research of the Office of Scientific Research and Development from 1941 to 1946 and was president of the National Academy of Sciences from 1947 to 1950.

Dr. Wolman Named Department Chairman.—Dr. Irving J. Wolman was named chairman of the department of pediatrics, the Graduate School of Medicine, University of Pennsylvania. Dr. Wolman will continue his duties at the Children's Hospital, where he is director of the division of hematology and blood bank and the division of microbiology and clinical pathology. He is editor of the *Quarterly Review of Pediatrics* and a member of the editorial staff, *American Journal of Medical Sciences.*

TEXAS

Neurological Symposium in Houston.—The eighth annual symposium of the Houston Neurological Society will be held in the Texas Medical Center March 10-12, 1960. This program will consist of two sections, the first devoted to "Prenatal and Perinatal Factors in Neurological Disease," and the second concerned with "Pathogenesis and Treatment of Hydrocephalus." Participants will include Dr. Samuel P. Hicks, Boston; Dr. Russell J. Blattner, Houston; Marjorie M. Nelson, Ph.D., Berkeley, Calif.; William F. Windle, Ph.D., Bethesda, Md.; George W. Anderson, Providence, R. I.; Donald Matson, Boston; and Robert H. Pudenz, Pasadena, Calif. Interested clinicians and research workers are invited to attend and participate in the discussions. Registration fee is $10.

Society News.—New officers of the Texas Academy of General Practice are: Dr. Ewing S. McLarty, Galveston, president; Dr. Edwin W. Schmidt, Pecos, vice-president; Dr. Jack M. Partain, San Antonio, president-elect; Dr. Lawrence W. Johnson, Houston, treasurer; and Mr. Donald C. Jackson, Austin, executive secretary.——Lieut. Col. Albert J. Bauer, assistant chief of Brooke Army Hospital's radiology service, is the newly elected president of the Civilian-Military Radiological Society of San Antonio. Other officers are Dr. Joe C. Rude, Austin, vice-president, and Dr. Hugo F. Elmendorf Jr., San Antonio, secretary-treasurer. The society meets the third Wednesday of each month at the Fort Sam Houston Officer's Club for dinner followed by x-ray film reading.

Personal.—Dr. Randolph Lee Clark Jr. director of the University of Texas M.D. Anderson Hospital and Tumor Institute in Houston, was installed as president of the Alumni Association of the Mayo Foundation for Medical Education and Research, Oct. 8. He succeeds Dr. James F. Weir, of Rochester, Minn.——Dr. Lawrence E. Lamb, San Antonio, was named director of consultative services at the

School of Aviation Medicine, Brooks AFB. Dr. Lamb is also chief of the school's department of internal medicine. The School of Aviation Medicine is the aeromedical indoctrination and research center of the USAF Air University, which has its headquarters at Maxwell AFB, Ala.

WASHINGTON

Personal.—Two physicians associated with Johns Hopkins University School of Medicine, Baltimore, were appointed to joint positions with King County Hospital and the University of Washington School of Medicine, Seattle. Dr. Robert G. Petersdorf, assistant professor of medicine at Johns Hopkins, will become director of the medical service at King County Hospital and associate professor of medicine at the medical school. Dr. James R. Cantrell, associate professor of surgery at Johns Hopkins, was named director of surgery at King County Hospital and professor of surgery at the university. Dr. Petersdorf will assume his new duties Jan. 1 and Dr. Cantrell on June 1 of next year.——Dr. John R. Hogness, medical director of the University of Washington Hospital, Seattle, was appointed assistant dean of the School of Medicine. Dr. Hogness assumed the post vacated Sept. 1 by Dr. James W. Haviland, who resigned to enter full-time practice. Dr. Hogness will continue as the hospital's medical director, dividing his time between the two positions.

WISCONSIN

Dr. Davis Goes to India.—Dr. Milton Davis Jr., of Madison, will leave in January for Ludhiana, Punjab, India, where he will work as a medical missionary at the Christian Medical College Hospital. A native of Midway, Ky., Dr. Davis had three years of training in anesthesia at the University of Wisconsin, after which he held teaching appointments at the universities of Illinois, Louisville, and Wisconsin. At the Christian Medical College Hospital, which is supported by the Indian government and interdenominational Protestant efforts, Dr. Davis will be engaged in clinical practice and teaching. His wife will help at the hospital as a secretary and his four children will accompany him, the three older ones attending Woodstock School, Mussoorie, India. Dr. Davis will be sponsored by the Board of Missions of the Methodist Church.

GENERAL

Study of Availability of Research Information.—The Institute for Advancement of Medical Communication was awarded a grant by the National Science Foundation for a study of "The Metabolism of New Scientific Information." The chief aim of this project is to investigate the processes by which new information resulting from cardiovascular and endocrine research becomes generally available to the scientific community. Dr. Richard H. Orr, New York City, executive director of the institute, will serve as principal investigator.

Rheumatism Meeting in Detroit.—The sixth interim scientific session, the 25th anniversary program, of the American Rheumatism Association will be held Dec. 11 at the Henry Ford Hospital, Detroit, under the presidency of Dr. Charley J. Smyth, Denver. Ten papers are scheduled for the two plenary sessions and a total of 24 papers will be presented at two morning (11 a. m.) and two afternoon (3:30 p. m.) concurrent sessions. Twenty-seven papers will be read by title. A banquet is planned for 7:30 p. m. For information, write Mr. G. W. Speyer, 580 Park Ave., New York 21, Executive Secretary.

Annual Institute of Group Psychotherapists.—The American Group Psychotherapy Association, Inc., will hold its fourth annual institute, stressing "The Group Therapist—His Personality, Training, and Functions," Jan. 27-28, 1960, at the Henry Hudson Hotel, 353 W. 57th St., New York City. The 17th annual conference of the association will follow on Jan. 29-30 at the Henry Hudson Hotel. For program information, write The American Group Psychotherapy Association, Inc., 1790 Broadway, New York City 19. Dr. Cornelius Beukenkamp Jr., Great Neck, N. Y., is chairman of the publicity committee.

Registry for Ophthalmologists and Otolaryngologists.—"To facilitate the growth of academic ophthalmology and otolaryngology in both clinical and basic science areas in the various medical schools and associated hospitals and institutions across the country," an Employment Registry for Scientists has been established by the American Academy of Ophthalmology and Otolaryngology. The registry will serve to aid in the placement of candidates completing training who desire academic and investigative positions and it will also facilitate the replacement of those already in such positions who desire to take a different position. The registry will be operated by the academy without fee or obligation. For information, write Dr. William L. Benedict, 15 Second Street, S. W., Rochester, Minn., Secretary-Treasurer.

Prizes for Monographs.—The American Academy of Arts and Sciences announced its monograph prizes for 1960, awarded annually to the authors of unpublished monographs, one each in the field of humanities, social sciences, and physical and biological sciences. For each of the three, $1,000 awards are given. Monographs are defined for the purposes of these awards as a "scholarly contribution to knowledge, too long for an article in a learned journal and too specialized for a general book." Recipients will be expected to make their own arrangements for publication. For information, write Committee on

Monograph Prizes, American Academy of Arts and Sciences, 280 Newton St., Brookline Station, Boston 46, Mass. The final date in 1960 for receipt of manuscripts by the committee is Oct. 1. Awards will be announced in December.

Psychoanalytic Meeting in New York City.—The fall meeting of the American Psychoanalytic Association is being held Dec. 4-6, at the Biltmore Hotel, New York City. Robert Waelder, Ph.D., of Philadelphia, will give the principal scientific address. The following panel discussions are scheduled:

The Role of the Dream in Child Analysis.
Psychoanalysis and Ethology.
An Examination of Nosology According to Psychoanalytic Concepts.
Theoretical and Clinical Aspects of Overt Male Homosexuality.

For information, write to the Acting Executive Secretary, 36 W. 44th St., New York 36.

New Journal of Neurology.—The World Federation of Neurology, international group representing neurology societies in 42 nations, announced its new medical journal, *World Neurology.* Scheduled for monthly publication beginning July, 1960, *World Neurology* medical papers will be printed in four languages—French, German, English, and Spanish. Editorial offices will be in the United States, and the journal will be published by Lancet Publications, division of Modern Medicine Publications, Inc., Minneapolis. Editor-in-chief is Dr. Charles M. Poser, University of Kansas School of Medicine, currently on leave as medical executive officer to the world federation. Associate editors are Dr. Pearce Bailey, director of international neurological research, National Institute of Neurological Diseases and Blindness, Bethesda, Md., and Dr. Ludo van Bogaert, Antwerp, president of the WFN. Medical authorities from 26 nations have been named to the editorial board and consulting editorships.

Two Physicians Win Medical Nobel Prize.—The 1959 Nobel Prize in medicine was awarded Oct. 15 to Dr. Severo Ochoa, of New York University College of Medicine, New York City, and Dr. Arthur Kornberg, Stanford University School of Medicine, Stanford, Calif. The two physicians, who will share the more than $42,000 cash award, were selected by the Swedish Royal Caroline Institute of Medicine and Physiology for the professional and monetary honors awarded since 1901 under the will of Alfred Nobel, the Swedish inventor of dynamite. The citation announced the prize was for the discoveries by Dr. Ochoa and Dr. Kornberg "of the mechanisms in the biological synthesis of ribonucleic acid and desoxyribonucleic acid." Dr. Kornberg was born in Brooklyn and Dr. Ochoa is a naturalized American born in Luarca, Spain.

Grants Available for Metabolism Research.—The National Vitamin Foundation announced that its current major interest is in the support of research, preferably on man, "most likely to advance our understanding of the diverse metabolic functions of the vitamins." The foundation encourages research on vitamin nutrition and metabolism in the areas of (1) mental health and (2) side-reactions due to drugs and invites applications for grants-in-aid of such research from interested and qualified investigators. The new research interests of the foundation do not eliminate consideration by the foundation of applications for grants-in-aid of research on other aspects of vitamin metabolism and nutrition. Application forms for grants-in-aid may be obtained from the offices of the foundation at 149 E. 78th St., New York 21. Action is taken on applications twice each year, in the spring and fall. For grants to be effective July 1, applications should be mailed to the foundation before the preceding March 1; for January grants, applications should be in the possession of the foundation by Sept. 1.

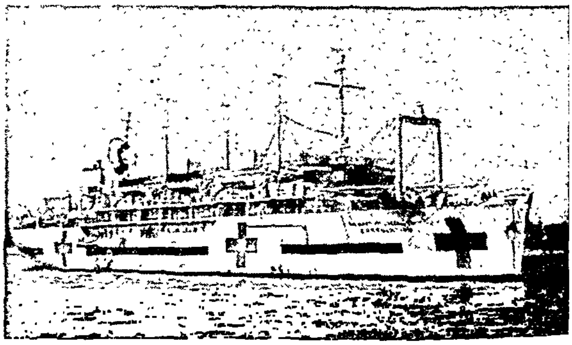
Award Offered by Obstetricians and Gynecologists.—The Central Association of Obstetricians and Gynecologists offers an annual award of $250 for outstanding investigative or clinical work in obstetrics and/or gynecology. Any accredited physician, research worker, or medical student living within the geographic confines of the association is eligible. Papers must be written expressly for this competition and they must be original, not having been previously presented or published. It is customary that the winning papers be presented at the annual meeting, the next of which will be held in Kansas City, Mo., Oct. 6-8, 1960. Manuscripts should be submitted to the secretary in triplicate, accompanied by an abstract not to exceed 150 words. No author's identification shall be shown on any of the three copies; the only identification shall be a covering letter addressed to the secretary. Manuscripts should be in the hands of the secretary by not later than July 6, 1960. For information, write Dr. Herman L. Gardner, secretary, 6410 Fannin St., Houston 25, Texas.

Television Program in Dallas.—A 30-minute television program, "The Other Side of the Sun," will originate from the 13th American Medical Association clinical meeting in Dallas for broadcast on stations in four cities. The program, one of the series of Merck, Sharp & Dohme "Ask Your Doctor" television reports, is presented in cooperation with the A. M. A. "The Other Side of the Sun," seen on Dec. 3 on KFJZ-TV Dallas–Fort Worth, and on KHOU-TV Houston, will also be shown at 8 p. m., Sunday, Dec. 6, on KPHO-TV (channel 5), Phoenix, Ariz., and at 10:30 p. m., Monday, Dec. 7, on KSL-TV (channel 5), Salt Lake City. Program material is based on the "Sunlight and the Skin" symposium, a special feature of the Dallas scientific exhibit program, sponsored by the A. M. A. Committee on Cosmetics. Featured on the program are Dr. James B. Howell, Dallas; Dr. Rudolf L. Baer, New York City; and Harold F. Blum, Ph.D., Bethesda, Md. Network television personality Don Herbert moderates "The Other Side of the Sun."

Diagnostic Study for Children with Convulsive Disorders.—Children suffering from convulsive disorders may now obtain a complete diagnostic work-up at the National Children's Rehabilitation Center, Leesburg, Va. Charles Kram, Ph.D., center director, said the new service was launched "in an attempt to make it possible for children to obtain a complete diagnostic study in one facility where reports on the numerous examinations can be pulled together and a course of future treatment can be developed." The new service is open to children between 7 and 18 years old from all parts of the country. The fee for the service will be determined by what each family can afford to pay. The remainder of the cost will be assumed by the Federal Association for Epilepsy, a charitable nonprofit organization with headquarters at 1720 F St., N. W., Washington, D. C. Application for the service can be made by parents or referring physicians by writing to the Office of Admissions, National Children's Rehabilitation Center, Leesburg, Va. The center's major project is to provide a residential treatment and rehabilitation program on a year-around basis for those children having seizures. The new diagnostic service will be carried out over a period of from 15 to 30 days, during which the child will remain in residence at the 200-acre center.

Scientists Meeting in Chicago.—The 126th meeting of the American Association for the Advancement of Science will be held at the Morrison Hotel, Chicago, Dec. 26-31. All 18 sections of the association will have programs and about 90 affiliated societies will participate. Symposiums to be presented include the following: How Attitudes Affect Disease Control, The Changing Role of Mortality in American Family Life, Population and World Economic Development, Space Medicine, Genetics of Behavior, and One's Teeth and Aging. The presidential address will be given by Wallace R. Brode, Ph.D., Washington, D. C. Nine awards will be announced, including two for the AAAS-Westinghouse Science Writing Awards. The AAAS is a nonprofit organization with a four-fold aim: To further the work of scientists, to facilitate cooperation among scientists, to make science more effective in promoting human welfare, and to increase public understanding of science. Headquarters are at 1515 Massachusetts Ave., N. W., Washington 5, D. C. The executive officer is Dael L. Wolfle, Ph.D. Sidney S. Negus, Ph.D., Medical College of Virginia, Richmond, is in charge of public information for the meeting.

Select Chief Medical Officer of Project HOPE.—Dr. Paul E. Spangler, of Monterey, Calif., has been selected as senior medical officer of Project HOPE, the undertaking which will send the hospital ship Consolation to Southeast Asia early next year in an effort to bring advanced medical training to the health professions of friendly countries overseas. The permanent hospital staff aboard ship will be made up of 15 physicians, 2 dentists, 20 nurses, and about 20 auxiliary medical personnel. In addition, about 35 physicians will be flown to the ship every four months on a rotating basis. A graduate of Harvard Medical School, Boston, Dr. Spangler, who is a diplomate of the American Board of Surgery, recently retired from the U. S. Navy. He had served as chief of surgery on the U. S. hospital ship Repose, a sister-ship of the Consolation. The 3.5 million dollars needed to operate the ship for a year is currently being raised through voluntary contributions by individuals, corporations, businesses, labor unions, and other groups throughout the country.



The USS Consolation, mothballed Navy hospital ship at anchor in San Francisco Bay.

Senate Study of International Health.—A review of the world health is being conducted by the Committee on Government Operations of the United States Senate. Under special legislation approved in August, 1958, this committee was directed to make a "comprehensive review of any and all matters relating to international health research, assistance, and rehabilitation." A one-year appropriation was approved in January for the study. The review is being carried out by a Standing Subcommittee on Reorganization and International Organizations, under the chairmanship of Senator Hubert H. Humphrey, of Minnesota. The Senate study has thus far issued five publications. It expects to issue as many as 15 more publications prior to a general report which it will file by Jan. 31, 1960. The five initial publications "International Medical Research," a 117-page history of discoveries in cancer, heart disease, arthritis, neurological and mental disorders, allergies and infectious diseases, and others; "Statutory Authority for Medical and Other Health-Related Research in the United States Government," 66 pages; "The Status of World Health," 81 pages of chart and text on the world-wide incidence of malaria, schistosomiasis, yaws, tuberculosis, trachoma, yellow fever, etc; Senator Humphrey's Personal Tribute and Report on the World Health Organization, 145 pages; and "Cancer—A World-Wide Menace," 40-page study showing unusual patterns on incidence of lung, breast, stomach, and other types of cancer in various countries. Each of the publications is available on request to the Committee in its office: Room 162, Old Senate Office Building, Washington 25, D. C.

Fellowships Available for Arthritis Study.—The National Foundation announced the availability of fellowships for clinical study in arthritis and related disease for physicians "who have an interest in rheumatic diseases and who intend to apply their knowledge of these diseases to clinical service, teaching, or research." Only physicians licensed, or eligible for licensure, to practice in the United States and who have had at least two years of specialty training acceptable to the appropriate American board (or equivalent training) are eligible. All applicants must be citizens of the United States. The candidate should propose a program of full-time study in a hospital (preferably university-affiliated) which offers a well-developed program in arthritis and related diseases. The major portion of his time should be spent in clinical service, but a small amount may be devoted to research and teaching. Fellowships are awarded for a minimum of one year but may be renewed. Financial support for the fellow is $4,500 a year with $540 allowed annually for each dependent. Annual increases of $480 are ordinarily granted. Under unusual circumstances higher stipends may be permitted. For a full academic program, complete tuition and fees are paid; for other programs, a sum not to exceed $1,250 including tuition may be arranged. Application must be received by Feb. 1 for consideration about May 1, 1960; by Aug. 1 for consideration Nov. 1, 1960; and by Nov. 1, for consideration Feb. 1, 1961.

Society News:—The **American Society of Clinical Hypnosis** held its second annual program in Chicago, Oct. 9-11. Dr. Milton H. Erickson, Phoenix, Ariz., was the retiring president. The new officers for 1959-1960 are: president, Frank A. Pattie, Ph.D., Lexington, Ky.; president-elect, Dr. Herbert Mann, San Jose, Calif.; and secretary, Dr. Seymour Hershman, One North Pulaski Rd., Chicago 24. The third annual meeting will be in August, 1960, at Miami, Fla.——Dr. Richard H. Barrett, Hanover, N. H., was elected a director of the **American Board of Anesthesiology** Oct. 2 to fill the vacancy created by the expired term of Dr. Curtiss B. Hickcox, Hartford, Conn. Dr. Robert D. Dripps, of Philadelphia, and Dr. Milton C. Peterson, of Kansas City, Mo., were reelected to four year terms as directors of the board. Officers for the year 1959-1960 were elected as follows: president, Dr. Frederick P. T. Haugen, Portland, Ore.; vice-president, Col. Harvey C. Slocum, M. C., U. S. Army, Galveston, Texas; and secretary-treasurer, Dr. Forrest E. Leffingwell, Glendale, Calif.——Officers for 1960 of the **American Society of Anesthesiologists, Inc.,** are: president, Dr. Leo V. Hand, Boston; president-elect, Dr. Joseph E. Remlinger Jr., Chicago; immediate past-president, Dr. Daniel C. Moore, Seattle; first vice-president, Dr. Kenneth K. Keown, Dallas, Texas; second vice-president, Dr. Oliver F. Bush, Columbia, Mo.; secretary, Dr. Robert L. Patterson, 612 Berkshire Dr., Pittsburgh 15; assistant secretary, Dr. Charles O. Hamilton, South Bend, Ind.; treasurer, Dr. Albert M. Betcher, New York City; and assistant treasurer, Dr. Edwin Emma, Flushing, N. Y.——The **Association of Clinical Scientists** elected and installed the following officers at the annual business meeting: president, Dr. George F. Stevenson, Chicago; vice-president, Dr. Herbert Derman, Kingston, N. Y.; and secretary-treasurer, Dr. Robert P. MacFate, Chicago. Dr. Frederick W. Sunderman, of Philadelphia, will continue as the director of education for the association.——At the annual meeting of the **American School Health Association** Oct. 18-23, the following officers were elected for the year October, 1959, to October, 1960: president, Lyda Smiley, R.N., M.A., La Mesa, Calif.; president-elect, Dr. Leland M. Corliss, Denver; vice-president in charge of program, J. Keogh Rash, H.S.D., Bloomington, Ind.; treasurer, Warren Southworth, Dr. P.H., Madison, Wis.; and executive secretary, Dr. Arville O. DeWeese, 515 E. Main St., Kent, Ohio.——Officers of the **Gastroenterology Research Group** for 1959-1960 are as follows: Dr. E. Clinton Texter Jr., Chicago, chairman; Dr. Albert I. Mendeloff, Baltimore, vice-chairman; and Dr. Nicholas C. Hightower Jr., Temple, Texas, secretary-treasurer.

FOREIGN

German Congress in Vienna.—The fifth congress of the German Society for Esthetic Medicine will be held in Vienna, Austria, May 26 to May 29, 1960. The scientific program will consider four main subjects:

Treatment of Burns with Special Consideration of Optimal Esthetic Results.
Vascular Diseases of the Extremities and Their Relations to Esthetics.
Allergy and Esthetic Medicine.
The Hair and Its Treatment.

Application for presenting papers should be made to the local office and should be addressed to Frau Dr. Antoine, Wien, Wickenburgasse 28 (Austria), or to the president of the society: Prof. Dr. H. Th. Schreus, Düsseldorf, Mohrenstrasse 5, Universitätshautklinik (Germany). Application for the presenting of papers should be made before Feb. 29, 1960.

Congress of Gastroenterology.—The International Congress of Gastroenterology, organized by the Society of Netherlands Gastroenterologists, will be held April 20-24, 1960, in Leyden, Netherlands. The congress program includes five working sessions of a half day each. There will also be a sixth working session specially devoted to questions concerning x-ray technique, which plays such an important part in gastroenterological work. The two main themes of the congress will be: (A) pathology, pathological physiology, clinical aspects of the small intestine; and (B) hepatitis, cirrhosis hepatitis, and their possible connection. There will be five panel discussions on the following subjects:

Colitis Ulcerosa.
Coma Hepaticum.
Hepatitis and Its Treatment.
Morbus Crohn.
Diagnosis and Treatment of Portal Hypertension.

English will be the leading language of the congress. English, French, or German may be spoken, with simultaneous interpretation available. For information, write The Secretariat, International Congress of Gastroenterology, 16 Lange Voorhout, The Hague, The Netherlands.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, June 24. Final date for filing application is January 10. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Oral.* San Francisco, March 30-April 1; New York City, Nov. 14-17. Closing date for filing application is Jan. 2 and July 1. *Written.* Oct. 17. Closing date for filing application is May 1. *Oral. Gastroenterology.* Philadelphia, March 11-12. Final date for filing application is January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: *Part I, Written.* Chicago, January 16. Candidates notified of their eligibility to participate in the Part I examination must submit their case abstracts within thirty days of notification of eligibility. *Part II, Oral.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications was Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Pediatrics: *Written.* Jan. 8. Final date for filing application for the written examination was Dec. 1. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Milwaukee, May 1960. Final date for filing application is January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Psychiatry and Neurology: New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Cincinnati, Spring 1960. Deadline for filing applications is Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Oral Examinations (Part II):* Boston, Dec. 14-15; Winston-Salem, No. Car., Jan. 18-19; New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, Feb. 12. Final date for filing application was Dec. 1. *Oral.* May 1960. Final date for filing application was Dec. 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

DEATHS

Baughman, Daniel Sparks Ⓜ Madison, S. D.; born in 1887; Chicago College of Medicine and Surgery, 1911; also a graduate in pharmacy; at one time taught at the Chicago College of Dental Surgery; formerly associated with the U. S. Public Health Service; past-president and vice-president of the South Dakota State Medical Association; past-president of the Madison District Medical Society and the Sioux Valley Medical Association; member of the American Academy of General Practice, American Association of Railway Surgeons, Association of Military Surgeons of the United States, and Medical Veterans of the World War; health officer of Lake County; associated with the Madison Community Hospital; died Sept. 12, aged 72.

Fife, James Douglas Ⓜ Colonel, U. S. Army, retired, Richmond, Va.; born in 1874; University of Virginia Department of Medicine, Charlottesville, 1897; commissioned in the medical corps of the U. S. Army in 1902; served in the Philippine insurrection and in World War I, when he was in charge of hospitalization with the American Expeditionary Force in France; retired June 30, 1938; recalled to active duty during World War II, retiring in 1946; held the Distinguished Service Medal and the Legion of Merit; died Sept. 17, aged 85.

Kanter, Joseph Ⓜ Chicago; born in Harrisburg, Pa., Dec. 1, 1897; University of Illinois College of Medicine, Chicago, 1929; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; veteran of World Wars I and II; retired from the Veterans Administration Dec. 31, 1955; formerly on the faculty of Marquette University School of Medicine in Milwaukee; served on the staffs of the Mount Sinai Hospital in Chicago and the Veterans Administration Hospital in Wood, Wis.; died in the Veterans Administration Westside Hospital Sept. 17, aged 61.

O'Brien, Gerald Francis Ⓜ New York City; Georgetown University School of Medicine, Washington, D. C., 1929; honorary police surgeon; associated with St. Clare's and St. Vincent's Hospital; died in Croton Falls, N. Y., Sept. 19, aged 57.

Pankey, Joseph Hamilton, Ferriday, La.; Atlanta College of Physicians and Surgeons, 1902; University of Nashville (Tenn.) Medical Department, 1909; fellow of the American College of Surgeons; past-president of the Quachita Parish Medical Society; coroner of Concordia Parish; served on the staff of the E. A. Conway Memorial Hospital in Monroe; associated with the Pankey Hospital in Ferriday and St. Francis Hospital in Monroe, where he died Sept. 9, aged 80.

Portwood, Hillary Armour Ⓜ Schlater, Miss. (licensed in Mississippi in 1913); died in the Greenwood-Leflore Hospital in Greenwood Sept. 9, aged 76.

Pound, William H., New York City; Baltimore Medical College, 1893; for many years deputy health commissioner; died in the Westchester Square Hospital Sept. 15, aged 92.

Raines, George Neely Ⓜ Captain, M. C., U. S. Navy, retired, Washington, D. C.; born in Jackson, Miss., April 2, 1908; Northwestern University Medical School, Chicago, 1931; interned at the U. S. Naval Hospital in Mare Island, Calif.; commissioned lieutenant (jg) in the medical corps of the U. S. Navy on June 26, 1930, and advanced progressively to the rank of captain to date from March 10, 1945; served aboard the USS Idaho, USS Saratoga, USS Lexington, and on destroyers as a general medical officer; first served as assistant to the Naval Unit, St. Elizabeth's Hospital, and as assistant chief of neuropsychiatry at the Old Naval Hospital; from 1943 to 1945 served as chief of neuropsychiatry at the U. S. Naval Hospital, Portsmouth, Va., where in the interim from 1953 to 1955 he served as executive officer and commanding officer, and the U. S. Naval Hospital in Bethesda, Md., from 1945 to 1950; from 1950 to 1953 and again from 1955 to 1958 served as head, neuropsychiatry branch, professional division, Bureau of Medicine and Surgery, Navy Department; hospitalized on June 1, 1958, and placed on the temporary disability retired list of the Navy on May 1, 1959; consultant in psychiatry, U. S. Public Health Service; professor and chairman of the department of psychiatry at the Georgetown University School of Medicine; an examiner of the American Board of Psychiatry and Neurology, of which he held various offices including that of president; chairman on the committee on nomenclature and statistics of the American Psychiatric Association from 1948 to 1954 and a member of the council in 1954; member of the American Neurological Association, American Academy of Neurology, Association for Research in Nervous and Mental Diseases, Washington Psychiatric Society, Washington Psychoanalytic Society, and the Medical Society of St. Elizabeth Hospital; fellow of the American College of Physicians; died in the U. S. Naval Hospital, Bethesda, Md., Sept. 16, aged 51.

Ⓜ Indicates Member of the American Medical Association.

Reaves, J. Ullman Ⓜ Mobile, Ala.; born in Anniston, Ala., July 30, 1885; Medical Department of Tulane University of Louisiana, New Orleans, 1908; in 1932-1933 vice-chairman of the Section on Urology of the American Medical Association; past-president of the Mobile County Medical Society; member of the Southeastern Surgical Congress and the American Urological Association and past-president of its Southeastern Branch; fellow of the International College of Surgeons and past-president of the Alabama Chapter; specialist certified by the American Board of Urology; associated with the Providence Hospital, where he was a member of the executive board; died Sept. 19, aged 74.

Remly, Thomas Donald Ⓜ Milwaukie, Ore.; Hahnemann Medical College and Hospital of Philadelphia, 1917; associated with the Holladay Park Hospital in Portland; died Sept. 10, aged 67.

Rex, Elmer Galen, McConnelsville, Ohio; Medical College of Virginia, Richmond, 1928; a member of the county board of health; on the staff of the Rocky Glen Sanatorium, where he died Sept. 8, aged 58.

Schnur, Jacob, New York City; Columbia University College of Physicians and Surgeons, New York City, 1925; specialist certified by the American Board of Anesthesiology; member of the American Society of Anesthesiologists; veteran of World War II; associated with the Lincoln Hospital; died in the Memorial Hospital Sept. 15, aged 58.

Schumer, Henry Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1906; consultant at the Bronx Hospital, where he served in various capacities; on the staff and chairman of the medical board of the Hebrew Home and Hospital for the Chronic Sick, where he died Sept. 22, aged 82.

Shaver, Murton Rene Ⓜ Topeka, Kan.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1930; specialist certified by the American Board of Neurological Surgery; formerly on the faculty of the University of Cincinnati College of Medicine and on the staff of the Cincinnati General Hospital; chief of neurology and neurosurgery at the Veterans Administration Hospital; died Sept. 8, aged 51.

Sitter, Stephen Christopher, Colonel, U. S. Army, retired, Veterans Home, Calif.; born in Oshkosh, Wis., Aug. 23, 1907; Marquette University School of Medicine, Milwaukee, 1933; veteran of World War II and a survivor of the Bataan death march and three years in a Japanese prison camp; entered the regular Army in 1935 and retired Jan. 31, 1952; awarded the Bronze Star, two Oak Leaf Clusters, Army Commendation Ribbon, and Presidential Unit Citation; certified by the National Board of Medical Examiners; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Academy of Neurology and the American Psychiatric Association; fellow of the American College of Physicians; in 1947-1948 on the faculty of Georgetown University School of Medicine in Washington, D. C.; from 1948 to 1952 chief of neurology at the Letterman Army Hospital in San Francisco; neurologist at the Veterans' Home of California; died Sept. 12, aged 52.

Stark, George John Ⓜ Reading, Pa.; Temple University School of Medicine, Philadelphia, 1934; veteran of World War II; served as county coroner; physician at the Berks County Prison; associated with the Reading Hospital; died Sept. 16, aged 50.

Torbett, John Walter Jr. Ⓜ Beaumont, Texas; Baylor University College of Medicine, Dallas, 1930; fellow of the American College of Physicians; interned at Kings County Hospital in Brooklyn, where he served as resident physician; died in Gilchrist Sept. 7, aged 54.

Vaiden, John Bolling Jr., Lawrenceville, Va.; Medical College of Virginia, Richmond, 1914; veteran of World War I; died in St. Elizabeth's Hospital, Richmond, Sept. 12, aged 71.

Veldhuis, John George, Winter Haven, Fla.; Detroit College of Medicine, 1898; for many years associated with the Indian Service of the Department of Interior; served a residency at the Montana State Hospital in Warmsprings; died Sept. 2, aged 87.

Wakefield, Robert Sylvester, Riverside, Calif.; Southwestern Medical School of the University of Texas, Dallas, 1953; veteran of World War II; interned at the General Hospital of Riverside County in Arlington; served a residency at the Kern General Hospital in Bakersfield; chief of pediatrics at Parkview Memorial Hospital; died Sept. 4, aged 34.

Waldrop, Jefferson Gideon Ⓜ Chapel Hill, Tenn.; Birmingham (Ala.) Medical College, 1915; died in the Gordon Hospital, Lewisburg, Sept. 9, aged 74.

Wertheimer, Henry William Ⓜ New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1906; died in the Harkness Pavilion, Columbia-Presbyterian Medical Center Sept. 18, aged 79.

Wixson, Roy Henry Ⓜ Niagara Falls, N. Y.; University of Buffalo School of Medicine, 1901; associated with the Memorial and Mount St. Mary's hospitals; member of the Niagara Falls Kiwanis Club; died Sept. 10, aged 81.

Zimmerman, Francis Buerk, Louisville, Ky.; University of Louisville School of Medicine, 1933; interned at St. Joseph's Hospital in Lexington, Ky.; served a residency at the Gill Memorial Eye, Ear and Throat Hospital in Roanoke, Va., and Louisville (Ky.) General Hospital; formerly on the faculty of his alma mater; on the staffs of Norton and St. Anthony hospitals; died Sept. 13, aged 51.

FOREIGN LETTERS

BRAZIL

Leprosy.—Dr. N. S. Campos called attention to the resistance of Mycobacterium leprae to treatment with sulfones. His belief has been confirmed by Dr. H. C. S. Araujo of Rio de Janeiro (*Arquivos Mineiros de Leprologia*, vol. 19, April, 1959) who reported the case of a man who took 951 injections or a total of 4,558 Gm. of diaminodiphenylsulfone in seven years. After 11 years of continuous treatment the patient's peripheral nerves and ganglions were apparently normal but there were scattered islets of alopecia and hypesthesia on the skin of the extremities and an acute rash on the chest and abdomen. Sections of the skin of the chest and the nasal mucosa showed numerous acid-fast bacilli. The author concluded that the Myco. leprae were sulfone resistant and that the disease was highly contagious.

Neurological Complications from Rabies Vaccine.—Drs. J. L. de Assis and G. H. Duchêne of São Paulo (*Arquivos de Neuro-Psiquiatria*, vol. 17, September, 1959) reported a series of 11 patients who had neuroparalytic complications after receiving antirabies vaccination. These complications were classified as diffuse acute encephalomyelopathy, transverse acute myelopathy, acute ascending myelopathy, radiculo-opticomyelopathy, radiculoneuritis, and acute multiple peripheral neuropathy. One group of patients was treated with ACTH and the other with antihistaminics, with essentially the same results.

Problems of Senescence.—At a meeting of the National Medical Academy in Rio de Janeiro in August, Dr. Rolando Monteiro discussed some problems of senescence, not including the problem of senility. These may involve disturbances of the collagen as manifested in chronic rheumatoid arthritis and arteriosclerosis. It has been shown that the main alteration of the collagen fibers, as seen in the electron microscope, is the loss of its helicoidal structure.

Strongyloidiasis.—Lima and Roithman (*O Hospital*) reported a series of 62 patients with strongyloidiasis. Most of them had no symptom that could be attributed to the worms. A few had epigastric pain and diarrhea, but this was not necessarily correlated with the strongyloidiasis. Hyperchlorhydria was a common finding in this series. The authors found no evidence of liver damage that could be attributed to the strongyloidiasis. The treatment was disappointing. The authors concluded that gentian violet was of no value. Only 17% of the patients were cured, but none was cured by using oxytetracycline.

Deep Mycoses.—According to Dr. Carlos da Silva Lacaz (*Revista de medicina tropical de São Paulo*, July-August, 1959) the deep mycoses are common in South America. Exceptions are the mycoses produced by Cerocosporalla and Basidiomycetes, which are not found in this continent. Two deep mycoses peculiar to South America are caused by Blastomyces brasiliensis and Paracoccidioides loboi. Cryptococcosis, chromoblastomycosis, and histoplasmosis are also found in South America. Coccidioidomycosis has not been found in Brazil, and in the other South American countries it does not represent an important problem. Rhinosporidiosis has been observed in Brazil. Sporotrichosis is common, mainly in Brazil, where it causes about 0.5% of all dermatoses. Actinomycosis is more frequently seen than maduromycosis and is usually produced by Actinomyces brasiliensis. Monosporium apiospermum, Cephalosporium falciforme, and Madurella grisea are frequently recovered from patients with maduromycosis.

CHILE

Malignant Hypertension.—Dr. M. Plaza de los Reyes and co-workers studied a series of 60 patients with malignant hypertension (*Rev. méd. Chile* 87:603, 1959). Of these, 42 were between 40 and 59 years of age. The most frequent clinical manifestations were retinopathy in 58, severe headache in 57, proteinuria and/or hematuria in 54, diastolic pressure over 130 mm. Hg in 51, azotemia in 34, and loss of weight in 29. A study of the cause revealed essential hypertension in 18, chronic pyelonephritis in 25, and chronic nephritis in 13. In the autopsy or biopsy specimens the most frequent findings were pyelonephritis, malignant nephrosclerosis, and chronic nephritis. Thirty-eight patients were treated with reserpine, methonium compounds, pentolinium, or chlorothiazide, and in most the diastolic pressure was lowered under 105 mm. Hg and the retinopathy improved or disappeared.

The items in these letters are contributed by regular correspondents in the various foreign countries.

DENMARK

Appendicitis.—After the therapeutic principles in acute appendicitis had been established and the mortality had been greatly reduced interest in this disease waned. Several of its problems are still unsolved, however, and despite the enormous literature that has accumulated on this subject there is still a conflict of opinion regarding the cause, age incidence, and sex ratio. For the period 1922-1953 Sven Müller (*Acta chir. scandinav.* 117:325-334, 1959) studied the cases of 3,989 males and 2,465 females. There was a marked male preponderence but the gravity of these grossly definite cases reflected by the perforation rate was the same in both sexes differing only by a small percentage within the various age groups. The age distribution and sex ratio of acute appendicitis could not be adequately reflected by curves representing only the macroscopically verifiable cases. A truer picture was obtained if the diagnosis was based also on clinical and histological findings.

This series was compared with a series of tonsillitis cases. In the first two years of life before chronic changes had occurred in the appendix or in the tonsils surgical appendicitis was extremely rare while true acute appendicitis like acute tonsillitis must be assumed to be common. In these first years of life there was a slight male preponderance in the incidence of tonsillitis. It could not be determined if the same applied to appendicitis but, if so, the difference was slight. In older children appendicitis showed a more abrupt rise in frequency and a more marked sex difference than tonsillitis. This difference proved to be due to the almost total absence of tonsillar abscesses in the first decade of life.

During the fertile period of life there was a conformity of frequency between the two diseases due to a pronounced increase in mild, subchronic cases among women. This resulted in both diseases in abolition of the quantitative male preponderance while a marked qualitative sex difference remained. These circumstances must be assumed to be related to the production of estrogens. Comparison with age curves showing estrogen excretion supported this assumption. The analysis of the frequency curves for these two diseases of lymphoid tissue, particularly their conformity during the fertile period, corroborated Sahli's theory on the close relationship of appendicitis and tonsillitis.

Parenteral Fluid Administration.—Administration of fluid parenterally for prolonged periods often presents difficulties because rapid development of superficial thrombophlebitis may occur even when isotonic fluids are used. Attempts have therefore been made to administer the fluids through a catheter inserted into either the superior or the inferior vena cava usually in the presence of severe oliguria or anuria. J. Lindenberg and co-workers (*Acta. chir. scandinav.* 117:342-345, 1959) introduced a catheter into the inferior vena cava in a series of 36 patients. Catheterization was performed more than once in a few patients because the catheter originally inserted became blocked. The catheters were left in place for an average of 11 (maximum 64) days. Infusion through the inferior vena cava was more convenient for the patient than infusion into a peripheral vein because it did not impede his movements so much. It was also possible to administer nutrients in a higher concentration than by infusion into a peripheral vein. The technique used involved only a slight risk of infection. The danger of thrombosis did not seem to be serious. The frequency of thrombosis might presumably be further reduced by using a soft nylon catheter instead of a polystan catheter. No serious complications occurred.

Nitromin for Cancer.—An important group of the drugs used against cancer are derivatives of nitrogen mustard, which by interference with the nucleic-acid metabolism of rapidly proliferating cells exert a harmful effect on the synthesis of proteins. Numerous animal experiments have shown the antineoplastic effect of these drugs both on transplanted sarcomas and carcinomas and on cellular suspensions injected either intraperitoneally or intravenously. Nitromin is less toxic and has a greater effect on cancer cells than nitrogen mustard.

N. Blixenkrone-Møller (*Acta chir. scandinav.* 117:189-196, 1959) used the drug on a series of 87 patients in relation to operations for carcinoma of abdominal organs. It was given intraperitoneally and intravenously. In 21 patients nausea and sometimes vomiting occurred shortly after the drug was injected. Persistent vomiting was observed in only two patients. Urticaria developed in one. In 16 slight motor agitation, clouded mentality, euphoria, or confusion occurred in relation to these injections but these reactions usually persisted for only one or two days and did not necessitate interruption of the treatment. In 15 patients severe motor agitation, confusion, and hallucinations occurred and these patients required constant supervision. In seven it was necessary to interrupt the treatment. In only 35 patients did no subjective discomfort develop in relation to the treatment. In 42 a fall in the leukocyte count to below 4,000 per cubic millimeter occurred often after a transient increase. In eight or nine patients the counts fell below 2,000. In 14 the platelet counts fell to below 100,000 during or after the treatment.

Of the 87 patients, 29 died in the hospital during or after treatment. Of the 39 patients whose condition was definitely inoperable, 15 died, and so did 14 of the 48 who were subjected to radical operation. An analysis of the causes of death in the 15 patients who were considered to be definitely inoperable did not disclose any evidence suggesting that the Nitromin was a contributing factor. Most of the patients died of cancer and the remainder died from pulmonary or cardiac complications. In the 14 patients who died after radical operation, the causes of death were those usually seen after such operations and in none could it be demonstrated that the drug had been a directly contributing factor, but the case fatality rate was so much higher than in the patients who did not receive Nitromin that the possibility could not be excluded that the drug might have lowered the resistance of the patients. The author concluded that Nitromin was highly toxic, that its use was not without hazards, and that it often proved impossible to complete the planned courses of treatment. Although it undoubtedly exerted an inhibitory action on the growth of human cancer cells, its high toxicity led the author to state that it could not be recommended for further use.

Total Gastrectomy for Carcinoma.—Of 358 patients with gastric carcinoma admitted to the surgical department of the Finsen Institute in Copenhagen during the period 1948 to 1957, 58 or 41% of those in whom the tumors could be removed had total gastrectomy, according to Zacho and Fischermann (*Acta chir. scandinav.* 117:278-294, 1959). Most of the patients selected had advanced or poor-risk cases, with tumors originating mostly from the upper or central portion of the stomach and often occupying the entire or almost entire stomach.

With the exception of the years 1949 and 1950 when the indications were more liberal total gastrectomy was performed only in the presence of tumors so widespread that no part of the stomach could be preserved. The primary postoperative mortality during the entire period was 28% for palliative and 9% for radical operations. In the last four years of the period of study after the preoperative and postoperative treatment had been greatly improved, the mortality was 13% and 0% respectively. The operative mortality depended chiefly on complicating diseases. In the present series all the deaths occurred in those in whom complicating diseases were present preoperatively. The next most important factor was the size of the tumor and its extragastric spread, i. e., the stage of the disease. The extent of the operation in terms of removed or resected organs did not influence the death rate, nor did the technical difficulties involved, as when the interposition method was used there were no deaths.

In the period 1948-1952 end-to-side and end-to-end esophagojejunostomy was used. The latter type gave better results early as well as late. All the five-year survivors had this type of anastomosis. In the period 1953-1957 the authors used direct esophagoduodenostomy and interposition of the transverse colon or jejunum between the esophagus and duodenum. The interposition procedure appeared to be most promising. It has not been associated with any operative deaths and the patients who had the radical operation have returned to work and to a normal life. Of the patients who survived palliative operations performed more than five years ago 25% were alive at the end of two years. Of those followed up 79% had enjoyed temporary freedom from symptoms and 29% had gone back to work for a time. One of the patients who had a "palliative" operation was still alive eight and one-half years after the operation and was fully able to work. Of the patients who survived radical operations performed more than five years ago 33% were still alive. They had negligible subjective complaints and were in good condition. All of them were able to work.

FINLAND

Herniation of Nucleus Pulposus.—A series of 324 patients with herniation of the nucleus pulposus, verified on operation, was analyzed by Troupp and Ulfves (*Nordisk medicin,* July 30, 1959). They excluded patients with recurrent protrusion, compression of the cauda equina, and high lumbar protrusion. In 190 patients the symptoms suggested involvement of only one root. When the signs and symptoms indicated involvement of several roots, diagnosis of the level of involvement on the basis of the clinical findings was generally so inaccurate that myelography was indicated. Myelography was also indicated for anomalies of the lumbar spine or when the level of disk degeneration did not tally with the clinically determined level. The diagnosis of a neurological level can never be exact, and even a radiologic diagnosis is not infallible, because lateral prolapses may compress a root without betraying themselves radiologically. Thus, certain conditions raise doubts and call for myelography before any operation is performed.

FRANCE

Congenital Toxoplasmosis.—M. Lelong and coworkers (*Archives françaises de pediatrie,* vol. 16, 1959) reported that the treatment of toxoplasmosis with sulfamerazine and pyrimethamine gave disappointing results in six patients with congenital toxoplasmosis. Two died, one is blind, one has an irreversible encephalopathy, one has severe brain lesions, and only one has normal psychomotor development. The spinal fluid in all these infants revealed a moderate lymphocytic reaction and hyperalbuminosis. Because of the poor results of treatment it is important to diagnose toxoplasmosis in the expectant mother. By treating the disease in the pregnant woman transmission to the infant might be prevented, but the diagnosis is often difficult because symptoms are discreet and may be mild or absent. The authors recommend making serologic tests for toxoplasmosis as close as possible to the beginning of pregnancy.

INDIA

Azacyclonol in Schizophrenia.—K. Bhaskaran and co-workers studied the effects of azacyclonol in five patients who had chronic schizophrenia with auditory hallucinations and delusions (*Journal of the Indian Medical Association*, vol. 33, Sept. 1, 1959). The duration of the illness in these patients varied from 1½ to 15 years. All had received electroconvulsive therapy, insulin, chlorpromazine, and reserpine without lasting benefit. Cingulectomy had been performed on one of the patients a few months before the trial without significant benefit. The patients were given 100 mg. of azacyclonol twice a day by mouth. The dose was gradually increased in the course of a week to a maximum of 200 mg. three times a day. It was continued for at least 30 days unless unpleasant side-effects or complications occurred. The longest period of administration was 41 days. The status with special reference to the hallucinations and delusions was reassessed at the end of treatment.

In three patients administration of the drug was discontinued due to the appearance of unpleasant side-effects or aggravation of symptoms. Thus, the patient who had undergone cingulectomy developed epileptiform convulsions on the ninth day of treatment while the clinical status and intensity of hallucinations and delusions remained unchanged. The clinical conditions and hallucinations were aggravated in two other patients after 14 and 12 days of treatment. The other two patients showed no significant change in their clinical condition and the nature of hallucinations and delusions in spite of receiving the drug for 36 and 41 days, respectively, in maximum doses of 600 mg. a day. No other side-effects except the epileptiform convulsions, seen in one patient, occurred and the blood findings and liver function tests were unaffected by the drug. The drug was thus of no value in chronic schizophrenia with hallucinations and delusions.

Amebic Dysentery.—B. Krishnakutty treated 17 patients who had amebic dysentery with a preparation containing 250 mg. of iodochlorohydroxyquin, 75 mg. of chloroquine, and 500 mg. of sulfadimidine per tablet. These components exert their action on the amebas in the intestine, extraintestinal amebiasis, and bacteria in the intestine respectively. Of the 17 patients, 15 showed active vegetative forms of Entamoeba histolytica in their stools. One revealed typical ulcerations in the large intestine on sigmoidoscopic examination while the last had Charcot-Leyden crystals in the stools. This was taken as presumptive evidence of amebic infection. One tablet three times a day after meals was given to all patients. Fifteen patients showed a good response within a week with disappearance of mucus, blood, and amebas from the stools and subjective clinical improvement. Two patients responded poorly and one of them had a relapse.

Pyloric Stenosis.—A. E. deSa reviewed a series of 31 patients with congenital hypertrophic pyloric stenosis (*Indian Journal of Child Health*, vol. 8, September, 1959). Of these, 29 were treated surgically—in most after a fair trial of medical treatment. The earliest time of onset of symptoms was the day of birth (three patients) and the latest 120 days (average 22.6 days). The average age at operation was 48.4 days. In 14 the pylorus was palpable clinically. On the operating table it was described as firm and fibromuscular in 13 patients, as showing muscular hypertrophy in 5, fibrous in 2, and gritty and cutting like an unripe pear in 2. In 6 patients the duodenal fornix was inadvertently opened. The only death in the series occurred in one of these. The average duration of postoperative vomiting was four days. All the children who survived were cured of their vomiting in 1 to 10 days. The author preferred operation for this condition to medical treatment as the prolonged nature of the latter exposes the child to the risk of intercurrent gastrointestinal and pulmonary infection and the fate of the medically treated pyloric "tumor" is debatable while after the Rammstedt operation a completely normal pylorus is left. The rapid return to normal health following operation is the most gratifying feature.

Barbiturates and Blood Sugar Levels.—Grewal and Deshpande (*Indian Journal of Medical Sciences*, vol. 31, August, 1959) studied the action of amobarbital, phenobarbital, and thiopental on the blood sugar level in rabbits. The drugs were given intravenously and blood samples were collected every 30 minutes for two hours. Amobarbital was given in doses of 20, 30, and 40 mg. per kilogram of body weight. On the smallest dose the blood sugar level was unchanged, but on the other two it was raised slightly. The response to 30 mg. per kilogram of body weight was, however, higher than to 40 mg. per kilogram of body weight. No anesthesia was produced in rabbits with doses of 20 and 30 mg. per kilogram of body weight, but with 40 mg. per kilogram anesthesia was produced for 20 to 30 minutes. Phenobarbital given in the same amounts did not significantly alter the blood sugar level. The smallest dose caused insignificant hypoglycemia and the other two caused insignificant hyperglycemia.

With thiopental, weak hyperglycemia occurred after a dose of 20 mg. per kilogram of body weight and this dose caused anesthesia for 10 to 15 minutes. None of the barbiturates used produced a potent hyperglycemic response. The anesthetizing action of amobarbital showed no relation to its action on blood sugar. Phenobarbital had no definite action on blood sugar but with thiopental the hyperglycemic response was comparable to its anesthestic action and the blood sugar rise was maximal under deep anesthesia while it diminished with recovery from the anesthesia. This difference in the actions of amobarbital and thiopental might be due to different modes of action of these drugs in raising the blood sugar level.

JAPAN

Effect of Surgery on Liver Functions.—According to Eguchi (*Acta medica*, July, 1958) the liver occupies a key position in postoperative tissue repairs. The author applied the sulfobromophthalein clearance test to a series of 18 patients whose operations included such major procedures as panhysterectomy and such relatively minor procedures as curettage. Observations were made on the first, third, fifth, and seventh postoperative days. The decline in liver function reached a peak on the first postoperative day. The more serious and involved the operation, the greater the decline in liver function. The author concluded that adequate measures to protect the liver should be taken in the preoperative and early postoperative periods, especially in patients whose liver function was somewhat impaired prior to operation.

Longevity.—The recent census for Japan showed a total population of over 90 million. This figure included 145 centenarians. In this group women outnumbered men by three to one and twice as many were living in the southwest where the climate is warmer than in the northeastern territories. In the main, the diet of these centenarians consists of rice, lentils, green vegetables, a moderate amount of fish, and hardly any red meats or dairy products. Theirs is essentially an outdoor life.

NORWAY

Hospital Infections.—The whole of volume nine (no. 7, 8, and 9) of the *Journal of the Oslo City Hospitals* for 1959 was devoted to an investigation by Dr. Knut Bie on resistant staphylococci and air-borne bacteria in the Ullevaal Hospital. In this hospital the incidence of hospital infections was once so low that in the period 1946 to 1953 there was only one such infection among 301 patients undergoing arthroplasty of the hip. When these infections became increasingly more frequent in spite of the precautions taken against them, a systematic study was undertaken of the 2,736 patients operated on between July 1, 1957, and June 30, 1958. Nose and throat cultures were taken of 258 members of the staff and of 49 student nurses. Over 600 samples were taken of the air, clothing, and linen. Among the patients 51 had postoperative wound infections due to resistant staphylococci. In 12 of these patients there was prolonged suppuration with distinct impairment of the patients' general condition. Among the 258 members of the staff examined 74 were found to harbor resistant staphylococci, and the percentage of carriers among the student nurses rose from 6 to 15 after four weeks of ward duty. Bie discussed such methods for the prevention of air-borne infections as ultraviolet radiation, chemical agents, dust suppression, and the treatment of carriers, but he warned that the effects of these methods can be evaluated only on the basis of prolonged observations.

Working Capacity and Angina Pectoris.—Between 1949 and 1958 angina pectoris or infarct of the heart was diagnosed at the Rikshospital in 650 patients. A questionnaire concerning their fitness for work and various other matters was sent to these patients. The answers received from 627 were analyzed by Dr. A. Ödegaard (*Tidsskrift for den norske laegeforening*, Aug. 15, 1959). All of them were taking anticoagulants regularly. The men were grouped in three classes according to whether their work was heavy, moderately heavy, or sedentary. The women were classified according to whether their employment was domestic or some other kind of work. Fitness for work was classified according to whether it was complete, partial, or nil. More than 67% were still at work many years after the diagnosis of their complaint—a finding agreeing with that of Master and Dack in the United States. Unfitness for work was four times more frequent among the heavy workers than among those whose work was sedentary. The author deplored the tendency for physicians to pamper patients who have angina pectoris who are thus encouraged to develop cardiac neuroses and to remain too long on sick leave.

Ethical Standards.—Dr. Odd Bjercke, secretary general of the Norwegian Medical Association, suggested that the association would do well to set its house in order now, before the country is faced by profound changes in the practice of medicine (*Tidsskrift for den Norske Laegeforening*, Aug. 15, 1959). At present there is a shortage of physicians, but those in practice have been trained at home under teachers with a comparatively uniform standard of medical ethics. Meanwhile about 700 Norwegian medical students are learning their art in foreign lands and they will outnumber the students studying medicine in Norway. When the exiles return to Norway, life is likely to be harder than it is now, and the maintenance of a high ethical code may be strained. Bjercke suggested that the association's present rules should be revised and expanded to meet the problems of today. Might not doctors, he asked, be enjoined constantly to keep their knowledge up to date and to share it with their patients and colleagues? Should not caution over clinical experiments and the employment of new methods of treatment be recommended? Rules for advertising and television publicity should be formulated. A committee should be created for the handling of disciplinary cases.

Vaccination Mishap.—In June, 1954, a Norwegian student wishing to take duty on a boat bound for America was told that he could not land there without having been vaccinated. Accordingly he submitted to vaccination which was followed in a few days by pain in his right arm, malaise, and headache. On his admission to the hospital he was found to have paralysis of both legs with loss of sensation below the umbilicus. During his subsequent hospital stay he developed various other ailments such as cystitis and, though he improved in certain respects in the following years, the degree of his invalidism in the summer of 1959 was estimated by experts at 35 to 40%. Vaccination being compulsory in Norway, the student was awarded compensation in September, 1959. At the law suit which led to this award it transpired that the vaccination had been carried out properly by a Norwegian physician and that the state must assume at least some of the costs of mishaps inevitable in the execution of measures for the benefit of the community as a whole.

Open-Heart Operations Under Hypothermia.—Since July, 1957, 25 patients at the Rikshospital in Oslo have undergone open cardiotomy under hypothermia for atrial septal defects with no operative deaths. Prof. Leif Efskind and co-workers (*Tidsskrift for den norske laegeforening*, Sept. 15, 1959) reported that the patients' ages ranged from 7 to 55, and in 16 the defects concerned the foramen ovale. There were four high and five low defects, all the high defects being combined with abnormalities of the pulmonary veins. The most common complications during the operations were arrhythmias, and to counter them infusions of oxygenated blood were given through the coronary arteries. Of late oxygenated blood has also been infused into the arch of the aorta with a view to supplying the brain with oxygen during the suspension of the circulation for three to eight minutes.

Auricular fibrillation was the most common of the arrhythmias but only in one patient did the fibrillation last more than a few days after the operation. Of the two patients who developed ventricular fibrillation it lasted only a few seconds in one. In the other it required defibrillation and cardiac massage to restore normal rhythm. The arrhythmias could hardly be attributed to the hypothermia, as they were just as common under ordinary anesthesia induced for operations on the heart. At a follow-up examination correction of the defects was found to be complete in 23 patients and in the other 2 it was incomplete. Most of the patients could be discharged from the hospital within a fortnight of the operation. As with other operations on the heart, the reactions to them were mildest in the patients under 15 years of age.

Serous Pleurisy.—Dr. P. Hoveid (*Nordisk medicin*, Nov. 10, 1959) reported a series of 100 patients with pleurisy who had been subjected to exploratory puncture. The pleural effusions found were serous or serohemorrhagic, and no patient who developed empyema was included. In 47 patients the effusion was traced to some infection, with tuberculosis definitely responsible in 16 and probably so in 22 others. Carcinomatosis was diagnosed in 21 patients, and this was the numerically most important diagnosis in patients over 50 years of age. Of the 43 patients under this age only 4 had carcinoma, whereas 30 had tuberculosis or a suspicion of it. In 20 patients the cause of the effusion remained obscure. Cultivation of the tubercle bacillus proved to be of limited value, whereas cytological examination of the effusion gave promising results with respect to malignant disease. There seems to be a great need for a rapid and reliable test for tuberculosis and in this respect Hoveid gives his experiences with needle biopsy of the parietal pleura carried out without any complications on 40 patients. Among these 9 had a diagnosis of tuberculosis and 14 a diagnosis of malignant disease. Though this simple test is useful with regard to both tuberculosis and malignant disease, it must be admitted that a histological examination of the parietal pleura throws little light on obscure causes of pleurisy.

PORTUGAL

Pulmonary Aspergillosis.—Tomé Vilar (*Gazeta med. portuguese* 12:132, 1959) described two new cases of pulmonary aspergillosis, both of which were recognized many years after a different diagnosis had been made. The first was that of a 10-year-old boy with tuberculosis who had a massive hemoptysis. At operation a granular mass was spilled from the cavity into the bronchial tree, killing the child by bronchial obstruction. The second was that of a woman whose condition was diagnosed as a lung abscess, but whose roentgenogram was atypical. At operation a putty-like mass was found in the abscess cavity. On microscopic examination the content of the cavities was found to be made up of mycelia with many dead and some calcified aspergilli. In both cases, in retrospect, the x-ray findings were found to be pathognomonic of pulmonary aspergillosis. Thus, it is seen that dead aspergilli may produce symptoms while acting purely as a foreign body. Another case was diagnosed preoperatively on the basis of the experience gathered from the study of the patients described above.

J. Cortez Pimentel (*Gazeta med. portuguese* 12:195, 1959) described anatomic and clinical findings which he believes might be interpreted as initial and residual stages of pulmonary aspergillosis. The initial stages were marked by the presence of mycelial masses, the size of which varied between that of a grain of corn and that of an olive, inside pulmonary cavities. This initial stage showed no clinical or radiologic manifestation and was identified in the course of a study of 205 specimens resulting from exereses made in connection with a research project. The residual stage may appear either in the form of a mycelial mass, necrosed and softened in the lumen or incorporated in the wall of an infected bronchiectatic pouch or a chronic lung abscess, or in the form of cavernoliths or broncholiths, formed by calcification of the fungus mass. The fact that some aspects, very much suspected of corresponding to residual stages of the aspergillosis, have been observed in bronchiectases of the lower lobes leads to the assumption that the frequency of this localization may be more common than is generally believed.

SWEDEN

Serum Transaminase Activity and Liver Damage.—Arturson and Persson (*Acta chir. scandinav.* 117:221-229, 1959) made serum glutamic-oxalacetic acid transaminase (SGO-T) activity determinations in combination with the common liver function tests on a single serum sample of each of 57 hospitalized patients with diseases of the biliary tract. In 15 liver biopsy was performed and the histological evaluation of the liver tissue was correlated to the SGO-T level. In all patients showing an increased SGO-T level the liver cells were more or less distintegrated due to an acute degenerative process. Hence the SGO-T level is a valuable index of acute liver cell destruction and seems to be useful especially for the differentiation of various types of biliary obstruction.

Fungi in Peptic Ulcers.—A series of 30 resected stomachs were examined for fungi by B. Holmström and co-workers (*Acta chir. scandinav.* 117:215-220, 1959). The operative specimens contained 22 gastric and duodenal ulcers, 12 of which showed growth of fungi. In 15 instances samples from the ulcer and adjacent mucosa were cultured concurrently. Growth of fungi was noted in four. The strains found were chiefly Candida albicans and Torulopsis glabrata which are saprophytes but potential pathogens. The authors drew attention to the possibility that the fungi might interfere with the healing of the ulcer and that the administration of broad-spectrum antibiotics favors the growth of the fungi.

Cineroentgenographic Studies of Gastrointestinal Motility.—With use of the cineroentgenographic technique with image amplifier, studies have been made of the motility pattern of the stomach, duodenum, and small intestine after administration of a contrast medium. Liljedahl and co-workers (*Acta chir. scandinav.* 117:206-214, 1959) reported a series of 22 patients with gastric or duodenal ulcer, 5 of whom had undergone partial gastrectomy with the Billroth 1 and 14 with the Billroth 2 operation and 2 of whom had had total gastrectomy. Six normal subjects without gastrointestinal complaints were used as controls. After the Billroth 1 operation the motility pattern of the stomach was found essentially to resemble that in healthy subjects. Thus motility was slight in the fundus, but deep waves of contraction were observed in the part corresponding to the pylorus. In the region of the gastroduodenostomy a "pyloric" mechanism had developed in which the part of the duodenum included in the anastomosis acted as a sphincter. Antiperistaltic movements in addition to normal peristalsis were visible in the duodenum.

A similar motility pattern was observed in patients in whom the Billroth 1 operation had been complemented by vagotomy. In most of the patients who had had the Billroth 2 operation the contrast medium passed through the stomach rapidly. Some retention of the medium in the stomach occurred only in patients with anteceliac gastroenterostomy. No definite difference was noted between patients with and without the dumping syndrome as far as passage through the stomach was concerned. A distinct difference was, however, observed with respect to peristalsis in the small intestine. Thus, when the contrast medium reached the small intestine peristalsis was much brisker in the patients with dumping syndrome than in those who were asymptomatic. After reoperation to construct a Billroth 1 type of anastomosis all the patients with the dumping syndrome became asymptomatic. From the point of view of gastrointestinal motility these patients did not differ from the others in whom Billroth 1 gastrectomy had been performed.

Gastrectomy with Jejunal Replacement.—Sture Hedenstedt (*Acta chir. scandinav.* 117:295-310, 1959) performed gastrectomy with jejunal replacement on a series of 70 patients. A slight modification of the Henley technique was used by the author, who first drew up the separated jejunal segment through the transverse mesocolon to the upper portion of the abdominal cavity and later tied off the mesenteric third of the proximal end of the jejunal segment and made an oblique resection. At the conclusion of the operation the jejunal segment was interposed between the gastric stump and the duodenum. Gastric ulcer was present in 38 patients, duodenal ulcer in 21, carcinoma of the stomach in 6, and dumping syndrome in 5. The dumping syndrome occurred in one patient who had a Billroth 1 operation and in four who had Billroth 2 operations with secondary jejunal replacement.

There were no deaths in the 64 patients with peptic ulcer. The blood chemistry and the patients' weights showed a striking tendency to remain within normal limits. Recurrences in the form of stomal ulcer supervened in 2 of 15 male patients edge up to date and to share it with their patients and colleagues? Should not caution over clinical experiments and the employment of new methods of treatment be recommended? Rules for advertising and television publicity should be formulated. A committee should be created for the handling of disciplinary cases.

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Open-Heart Operations Under Hypothermia.—Since July, 1957, 25 patients at the Rikshospital in Oslo have undergone open cardiotomy under hypothermia for atrial septal defects with no operative deaths. Prof. Leif Efskind and co-workers (*Tidsskrift for den norske laegeforening*, Sept. 15, 1959) reported that the patients' ages ranged from 7 to 55, and in 16 the defects concerned the foramen ovale. There were four high and five low defects, all the high defects being combined with abnormalities of the pulmonary veins. The most common complications during the operations were arrhythmias, and to counter them infusions of oxygenated blood were given through the coronary arteries. Of late oxygenated blood has also been infused into the arch of the aorta with a view to supplying the brain with oxygen during the suspension of the circulation for three to eight minutes.

Auricular fibrillation was the most common of the arrhythmias but only in one patient did the fibrillation last more than a few days after the operation. Of the two patients who developed ventricular fibrillation it lasted only a few seconds in one. In the other it required defibrillation and cardiac massage to restore normal rhythm. The arrhythmias could hardly be attributed to the hypothermia, as they were just as common under ordinary anesthesia induced for operations on the heart. At a follow-up examination correction of the defects was found to be complete in 23 patients and in the other 2 it was incomplete. Most of the patients could be discharged from the hospital within a fortnight of the operation. As with other operations on the heart, the reactions to them were mildest in the patients under 15 years of age.

Serous Pleurisy.—Dr. P. Hoveid (*Nordisk medicin*, Nov. 10, 1959) reported a series of 100 patients with pleurisy who had been subjected to exploratory puncture. The pleural effusions found were serous or serohemorrhagic, and no patient who developed empyema was included. In 47 patients the effusion was traced to some infection, with tuberculosis definitely responsible in 16 and probably so in 22 others. Carcinomatosis was diagnosed in 21 patients, and this was the numerically most important diagnosis in patients over 50 years of age. Of the 43 patients under this age only 4 had carcinoma, whereas 30 had tuberculosis or a suspicion of it. In 20 patients the cause of the effusion remained obscure. Cultivation of the tubercle bacillus proved to be of limited value, whereas cytological examination of the effusion gave promising results with respect to malignant disease. There seems to be a great need for a rapid and reliable test for tuberculosis and in this respect Hoveid gives his experiences with needle biopsy of the parietal pleura carried out without any complications on 40 patients. Among these 9 had a diagnosis of tuberculosis and 14 a diagnosis of malignant disease. Though this simple test is useful with regard to both tuberculosis and malignant disease, it must be admitted that a histological examination of the parietal pleura throws little light on obscure causes of pleurisy.

PORTUGAL

Pulmonary Aspergillosis.—Tomé Vilar (*Gazeta med. portuguese* 12:132, 1959) described two new cases of pulmonary aspergillosis, both of which were recognized many years after a different diagnosis had been made. The first was that of a 10-year-old boy with tuberculosis who had a massive hemoptysis. At operation a granular mass was spilled from the cavity into the bronchial tree, killing the child by bronchial obstruction. The second was that of a woman whose condition was diagnosed as a lung abscess, but whose roentgenogram was atypical. At operation a putty-like mass was found in the abscess cavity. On microscopic examination the content of the cavities was found to be made up of mycelia with many dead and some calcified aspergilli. In both cases, in retrospect, the x-ray findings were found to be pathognomonic of pulmonary aspergillosis. Thus, it is seen that dead aspergilli may produce symptoms while acting purely as a foreign body. Another case was diagnosed preoperatively on the basis of the experience gathered from the study of the patients described above.

J. Cortez Pimentel (*Gazeta med. portuguese* 12:195, 1959) described anatomic and clinical findings which he believes might be interpreted as initial and residual stages of pulmonary aspergillosis. The initial stages were marked by the presence of mycelial masses, the size of which varied between that of a grain of corn and that of an olive, inside pulmonary cavities. This initial stage showed no clinical or radiologic manifestation and was identified in the course of a study of 205 specimens resulting from exereses made in connection with a research project. The residual stage may appear either in the form of a mycelial mass, necrosed and softened in the lumen or incorporated in the wall of an infected bronchiectatic pouch or a chronic lung abscess, or in the form of cavernoliths or broncholiths, formed by calcification of the fungus mass. The fact that some aspects, very much suspected of corresponding to residual stages of the aspergillosis, have been observed in bronchiectases of the lower lobes leads to the assumption that the frequency of this localization may be more common than is generally believed.

SWEDEN

Serum Transaminase Activity and Liver Damage.—Arturson and Persson (*Acta chir. scandinav.* 117:221-229, 1959) made serum glutamic-oxalacetic acid transaminase (SGO-T) activity determinations in combination with the common liver function tests on a single serum sample of each of 57 hospitalized patients with diseases of the biliary tract. In 15 liver biopsy was performed and the histological evaluation of the liver tissue was correlated to the SGO-T level. In all patients showing an increased SGO-T level the liver cells were more or less distintegrated due to an acute degenerative process. Hence the SGO-T level is a valuable index of acute liver cell destruction and seems to be useful especially for the differentiation of various types of biliary obstruction.

Fungi in Peptic Ulcers.—A series of 30 resected stomachs were examined for fungi by B. Holmström and co-workers (*Acta chir. scandinav.* 117:215-220, 1959). The operative specimens contained 22 gastric and duodenal ulcers, 12 of which showed growth of fungi. In 15 instances samples from the ulcer and adjacent mucosa were cultured concurrently. Growth of fungi was noted in four. The strains found were chiefly Candida albicans and Torulopsis glabrata which are saprophytes but potential pathogens. The authors drew attention to the possibility that the fungi might interfere with the healing of the ulcer and that the administration of broad-spectrum antibiotics favors the growth of the fungi.

Cineroentgenographic Studies of Gastrointestinal Motility.—With use of the cineroentgenographic technique with image amplifier, studies have been made of the motility pattern of the stomach, duodenum, and small intestine after administration of a contrast medium. Liljedahl and co-workers (*Acta chir. scandinav.* 117:206-214, 1959) reported a series of 22 patients with gastric or duodenal ulcer, 5 of whom had undergone partial gastrectomy with the Billroth 1 and 14 with the Billroth 2 operation and 2 of whom had had total gastrectomy. Six normal subjects without gastrointestinal complaints were used as controls. After the Billroth 1 operation the motility pattern of the stomach was found essentially to resemble that in healthy subjects. Thus motility was slight in the fundus, but deep waves of contraction were observed in the part corresponding to the pylorus. In the region of the gastroduodenostomy a "pyloric" mechanism had developed in which the part of the duodenum included in the anastomosis acted as a sphincter. Antiperistaltic movements in addition to normal peristalsis were visible in the duodenum.

A similar motility pattern was observed in patients in whom the Billroth 1 operation had been complemented by vagotomy. In most of the patients who had had the Billroth 2 operation the contrast medium passed through the stomach rapidly. Some retention of the medium in the stomach occurred only in patients with anteceliac gastroenterostomy. No definite difference was noted between patients with and without the dumping syndrome as far as passage through the stomach was concerned. A distinct difference was, however, observed with respect to peristalsis in the small intestine. Thus, when the contrast medium reached the small intestine peristalsis was much brisker in the patients with dumping syndrome than in those who were asymptomatic. After reoperation to construct a Billroth 1 type of anastomosis all the patients with the dumping syndrome became asymptomatic. From the point of view of gastrointestinal motility these patients did not differ from the others in whom Billroth 1 gastrectomy had been performed.

Gastrectomy with Jejunal Replacement.—Sture Hedenstedt (*Acta chir. scandinav.* 117:295-310, 1959) performed gastrectomy with jejunal replacement on a series of 70 patients. A slight modification of the Henley technique was used by the author, who first drew up the separated jejunal segment through the transverse mesocolon to the upper portion of the abdominal cavity and later tied off the mesenteric third of the proximal end of the jejunal segment and made an oblique resection. At the conclusion of the operation the jejunal segment was interposed between the gastric stump and the duodenum. Gastric ulcer was present in 38 patients, duodenal ulcer in 21, carcinoma of the stomach in 6, and dumping syndrome in 5. The dumping syndrome occurred in one patient who had a Billroth 1 operation and in four who had Billroth 2 operations with secondary jejunal replacement.

There were no deaths in the 64 patients with peptic ulcer. The blood chemistry and the patients' weights showed a striking tendency to remain within normal limits. Recurrences in the form of stomal ulcer supervened in 2 of 15 male patients with duodenal ulcer. These healed immediately after vagotomy. In men with duodenal ulcer the resection should be extremely high or preferably moderate and combined with vagotomy. Dumping syndromes of the severest grade in four patients who had the Billroth 2 and one who had the Billroth 1 operation disappeared immediately and completely after secondary jejunal replacement. In one patient who had the Billroth 2 operation and who was an alcoholic the symptoms were absent only when he abstained from alcohol. The author stated that a jejunal segment 15 cm. long anastomosed between the gastric stump and the duodenum was regularly independent of its mesenteric supply after three months.

Svante Annersten (*Acta chir. scandinav.* 117:311-315, 1959) studied a series of 46 patients (19 with gastric ulcer, 25 with duodenal ulcer, and 2 with the dumping syndrome), all treated with jejunal replacement by Henley's method. Two deaths were due to complications not connected with the replacement technique. On follow-up after one to six months only three patients had dumping syndromes and these were mild. Only three patients could not tolerate milk, the substance most commonly eliciting dumping. One recurrence was recorded. Gastric resection with jejunal replacement offered the following advantages over the Billroth 1 operation: The formation of a reservoir delaying the passage of the gastric contents decreased the danger of the dumping syndrome. A really high resection was possible without danger of tension, thus reducing the frequency of recurrences. The jejunoduodenal anastomosis was technically simpler than the gastroduodenostomy since the lumens were of the same caliber and the duodenum needed not be mobilized so far distally with attendant danger of damage to the pancreas. End-to-side anastomosis was also possible. Anastomosis between the whole circumference of the gastric incision and the jejunal segment presented no difficulty.

Compared with the Billroth 2 resection the technique offered the following advantages: The food entering the jejunum had already undergone duodenal digestion with pancreatic enzymes and bile in the normal manner. The danger of anemia might also be decreased owing to better iron absorption. No dangerous stagnation occurred in the duodenal stump which had in many patients proved permeable to bacteria even in the presence of intact sutures. The incidence of the dumping syndrome was also appreciably lower.

Adrenal Cortical Tumors.—G. Birke and co-workers (*Acta chir. scandinav.* 117:233-246, 1959) treated nine patients aged 34 to 73 for tumors emanating from adrenal cortical tissue. Four of the tumors showed definite hormonal activity. In a fifth there was doubt in this respect. An important finding was the close correlation between the adrenal cortical tumors and demonstrated hormonal activity. Adrenal cortical tumors should be extirpated when possible; if this is done in time the prognosis is good. In five patients the tumor was located prior to operation. The operation was performed with the patients in the lateral nephrectomy position and the involved region was explored through a conventional lumbar renal incision. This was extended when necessary ventrally toward the midline and dorsally by division of the 11th and 12th ribs at the costal angles. When the tumor was large the peritoneum was opened to allow the intraperitoneal organs to be freed under direct vision. This incision provided good access to the tumor in all cases. During the operation and in the immediate postoperative period the patients required an extra supply of the steroids which normally were secreted by the adrenal cortex.

The authors further stated that hormonally active adrenal cortical tumors frequently resulted in atrophy of the nontumorous adrenal cortex. When the tumor has been extirpated the atrophic cortex cannot supply the increased amount of steroids that is necessary for normal postoperative recovery.

Of the nine patients four developed metastatic spread. One patient died of malignant hypertension probably induced by a hormonally active tumor. Another patient died of postoperative adrenal insufficiency. The three remaining patients were alive and asymptomatic one to four years after operation. Patients with adrenal cortical tumors face two dangers. One is, as in those with other tumors, metastatic spread; the other is the hormonal activity of the tumor. In both respects early treatment increases the prospect of good results. The authors concluded that hormonally inactive tumors generally were not diagnosed until they were relatively advanced and therefore frequently had metastasized. Hormonally active tumors become manifest at an earlier stage and, now that adrenal insufficiency can be compensated, have a more favorable prognosis.

Avulsion Fracture of the Os Calcis.—Avulsion fracture of the os calcis is a rare injury. Three cases were described by Arner and Lindholm (*Acta chir. scandinav.* 117:258-260, 1959). The mechanism of fracture in these patients did not differ from that in subcutaneous rupture of the tendo achillis. As regards the injury sustained each of these patients represented one of the types which can cause total rupture of this tendon. The clinical and roentgenographic features of all three were uniform. In each only a small part of the tendon had ruptured while the rest was intact and obviously of such tenacity that the injury caused avulsion of the actual attachment of the tendon. The degenerative changes which were demonstrated in the ruptured part of the tendon were identical with those found in tendon tissue which was totally ruptured. Histological study of the nonruptured part of the tendon showed normal appearance. The authors concluded that a normal tendo achillis probably could not be ruptured by indirect violence.

Severe Head Injuries.—Continuous improvements in treatment—shock therapy, antibiotics, respiratory aids such as tracheotomy, and hypothermia—have increased the chances of survival for persons with severe head injuries. Erik Åkerlund (*Acta chir. scandinav.* 117:275-277, 1959) investigated a series of 26 patients who had severe head injuries and who survived after having been unconscious for a week or more. The duration of unconsciousness was 1 week in 11 of these patients, 2 weeks in 7, 3 weeks in 4, and 4 to 10 weeks in 4. At follow-up one to six years later, eight of the patients were subjectively and objectively fully rehabilitated. Eight others had residual symptoms but returned to the work they did before the accident. Ten patients had more or less reduced working capacity due to sequelae of the head injury. Comparison with the duration of unconsciousness suggested that unconsciousness lasting up to four weeks was compatible with good restitution in about 67% of cases, particularly in young persons. When consciousness had been lost for more than a month severe residual defects seemed to be unavoidable.

Lymphography of Varicose Veins.—A series of 44 legs in 25 patients with varicose veins were studied by Jacobsson and Johansson (*Acta chir. scandinav.* 117:346-350, 1959) who used lymphography. The contrast medium was injected directly into lymph vessels which had been exposed distally in the legs. Prior to exposure these vessels had been rendered visible by subcutaneous injection of patent blue violet. Of the 25 patients, 10 of whom had varicosities with slight dependent edema which disappeared when the leg was elevated but no history of thrombosis or ulcer. In the other 15 patients the varicose veins were complicated by ulcer, thrombosis, or both. Altered lymph vessels were fairly unusual in legs with uncomplicated varicose veins but were more common when varicosity was accompanied by ulcer. The connection between the varicose ulcer and the lymphatic changes was obscure. The impaired circulation of the lymph and tendency to edema might predispose to ulcer. Also the constant infection in the ulcer might secondarily involve the lymphatics. Opposed to the first possibility was the observation that ulcers never occurred in patients with lymphedema in which the lymph circulation was impaired. The second alternative was the finding of lymphatic changes in limbs with uncomplicated varices.

UNITED KINGDOM

Ideal Flooring for Hospitals.—An investigation to find a durable, quiet, and nonslippery hospital floor covering is being sponsored by King Edward's Hospital Fund at Ashford Hospital, Middlesex. A long corridor has been divided into 10 55-ft. sections. Each has been covered with a different type of flooring. An investigation of wood flooring is being made at St. Peter's Hospital, Chertsey, and another into the best kind of flooring for aged patients at the West Middlesex Hospital, Isleworth. Highly polished hospital floors are now recognized as a source of danger. In recent years many limbs have been broken as a result of patients and attendants slipping on shiny floors. Yet hospitals must be kept clean. Ideally, flooring should also be long-lasting, attractive in appearance, easy to maintain, resistant to marking, and capable of withstanding heavy traffic.

For the 10 new kinds of flooring at Ashford Hospital 30 leading manufacturers were invited to submit samples. The flooring materials chosen included various compositions, a cork tile, linoleum sheet, linoleum tile, rubber sheet, rubber tile, and other forms of tile. Five service companies were invited to submit schedules and estimates for a basic system of maintenance that could be applied to the 10 different sections. The maintenance program will consist initially of thorough washing down, followed by the application of two coats of resin emulsion sealer. Daily maintenance will consist of sweeping with impregnated mop sweepers. Twice weekly there will be dry cleaning with emulsion polish. At the end of each quarter the corridor will be completely cleaned again and the cycle started afresh with two new coats of emulsion sealer.

Tests for Phenylketonuria.—The early diagnosis of phenylketonuria permits the treatment of infants with this metabolic error with diets low in phenylalanine to prevent or minimize mental deterioration. It is also important to differentiate phenylketonuria from other and untreatable forms of mental deficiency. Gibbs and Woolf (*Brit. M. J.* 2:532, 1959) made a phenylketonuria detection drive in Cardiff, where over a period of a year every mother of every child born in the city was asked to bring a specimen of the baby's urine to the infant welfare clinic when the baby was 3 weeks old, or as soon as possible after this. Bottles containing a litttle chlorobutanol as preservative were given to all the mothers. A 5% solution of ferric chloride was added to the urine until a definite color appeared. More recently a test paper known as Phenistix has been used. Many mothers stated that they were unable to get a urine specimen at such an early age, and only 1,192 were collected and tested; 51 of these were too alkaline to test and of the remaining specimens one gave a positive test for phenylpyruvic acid. Phenylketonuria was confirmed by chromatography of the serum for phenylalanine. Treatment with use of a diet low in phenylalanine was started when the baby was one month old and when it was 12 months old the IQ was 94.

Seven other infants passed urine that gave a green color with use of ferric chloride, exactly like that given by phenylpyruvic acid. Laboratory investigations showed that the reaction was not due to phenylalanine, but to the presence of p-hydroxyphenylpyruvic acid. In addition to the detection program in infants, all the children attending a junior school for the educationally subnormal had their urines tested. Of 279 children, two were found to have phenylketonuria, but one was 13 years of age, and the mental deterioration was too advanced for treatment.

Phenylpyruvic acid may not appear in patients with phenylketonuria until the child is 1 to 6 weeks old. By then it may have left the hospital, and the greater the delay in diagnosis the more difficult treatment becomes. The authors suggested testing the urines of all children for phenylpyruvic acid when they are 3 weeks old and again at 2 months of age. The difficulty of obtaining urine specimens, which appeared to be the chief obstacle in infants, could be overcome by applying test papers to the wet diapers. The diagnosis must always be confirmed by estimating the serum phenylalanine level. A diet containing large amounts of tyrosine or phenylalanine may result in the appearance of p-hydroxyphenylpyruvic acid in the urine, which is indistinguishable from phenylpyruvic acid if the ferric chloride test is used. The former acid is of no pathological significance.

Increase in Traffic Accidents.—A disturbing increase in the number of traffic accidents last summer was reported by the Minister of Transport. In July 588 persons were killed and 7,879 seriously injured, an increase of 16 and 21%, respectively, on the figures for July, 1958. Casualties among motorcyclists were particularly heavy. They suffered 10,513 casualties, an increase of over 30%, and 200 were fatal. This latter figure represents over 33% of all road deaths. Casualties among pedalcyclists fell from 5,557 to 5,343, but 64 were fatal. The total number of casualties to drivers of cars and other vehicles and to their occupants was 10,995, an increase of 1,036. Of these 155 were fatal. An increasing number of pedestrian casualties on the roads were reported, but fewer deaths—145 compared with 174 in the same period last year. During the first seven months of 1959 the total number of road casualties was 18,212, a rise of 11% over the figure for the corresponding period in the previous year. Fatal casualties rose by 137 to 3,245. The increase in traffic, about 12%, should be taken into consideration in interpreting these figures.

Goiter Caused by Asthma Remedy.—A popular remedy for asthmatic patients (Felsol) contains acetophenetidin, antipyrine, caffeine, extract of grindelia, and a compound of antipyrine with iodine (iodopyrine). This drug is considered by Morgans and Trotter (*Lancet* 2:374, 1959) to be potentially goitrogenic. Three adults developed goiters while taking Felsol powder for asthma, and a baby whose mother took the preparation during pregnancy was born with a goiter. The goiters were attributed to the action of iodopyrine, which contains 12 mg. of iodine per dose. This was confirmed by giving the adult patients similar powders which contained no iodopyrine, whereupon their goiters decreased in size. The baby's goiter disappeared spontaneously, as it was bottle fed.

Investigations with tracer doses of I^{131} in 10 asthmatic patients showed that iodopyrine in single doses of 5 to 60 mg., which are well within the therapeutic range, can inhibit the organic binding power of iodine. None of the other constituents of Felsol had this property. This work was confirmed in the rat by Brownstone and Pitt-Rivers (*Lancet* 2:376, 1959) who showed that iodopyrine, but not antipyrine alone, prevented the incorporation of I^{131} into body proteins. Iodopyrine also caused a lowering of the BMR. It would appear that the iodine in iodopyrine is quickly released and has a goitrogenic effect.

Staphylococcic Pneumonia and Skin Infection.—Secondary bacterial infection of the lung is still the most common cause of death in influenza pandemics. The epidemiologic pathway of the staphylococci in staphylococcic pneumonia secondary to influenza was investigated by Goslings and coworkers (*Lancet* 2:428, 1959). Strains of staphylococci were isolated from the sputums or postmortem material of patients in whom the diagnosis of Asian influenza had been established. The causative staphylococci were also isolated from skin lesions if present, or from the nose, on the assumption that the nasal strains are frequently identical with those causing skin lesions. In 40 patients who had influenza with secondary staphylococcic pneumonia, an antecedent staphylococcic cutaneous or other open lesion was found in 35%, and in a further 20% such an association seemed probable. Although only about a 33% of the patients with influenza had definite staphylococcic skin lesions there was a high incidence in such lesions in other members of the household or in close contacts, such as nurses. Resistance to antibiotics increased after hospitalization of the patients. Phage-typing showed a marked increase of group 3 strains in cultures isolated after the first day.

It was suggested that all staphylococcic lesions, particularly furunculosis, should be treated with the utmost care in influenza pandemics, and that if a member of a family which harbors staphylococci contracts influenza the patient should be watched carefully for any sign of secondary lung infection. This also suggests that the sputum of influenzal patients with pneumonia as a complication should be repeatedly cultured.

Desoxyribonucleic Acid Content of Cancer Cells.—Stich and co-workers claim to have improved the accuracy of the histological diagnosis of cancer by direct measurement of the desoxyribonucleic acid (DNA) content of individual nuclei in cancer cells

(*Lancet* 2:385, 1959). The excised tissue was fixed, sectioned, hydrolyzed with normal hydrochloric acid, and stained in leukobasic fuchsin. The DNA content of the nuclei of individual epithelial cells, in metaphase and telophase, was then measured spectrophotometrically. Initially the levels in about 30 nuclei were averaged in the cells of 8 specimens of normal colonic mucosa, 29 benign colonic polypi, and 23 colonic adenocarcinomas. The DNA content was measured in arbitrary units. The benign polypi nuclei averaged 12 DNA units. Carcinoma cells gave abnormal values, centering around 16 or 21 DNA units, and occasionally multiples of these numbers. No abnormal values were found in the nuclei of cells of the epithelium of normal colon or histologically benign polypi. There was correlation between the histological grade of malignancy of a carcinoma and the nucleic DNA value. Carcinomas of the bronchus, stomach, and female breast were also found to give abnormal nucleic DNA values.

Because of the clear-cut results, the nuclei of epithelial cells in another series of tumors were examined, the DNA content of only three nuclei being measured. The results averaged the same as when 30 nuclei were counted. No histologically benign tissues were found to possess the abnormal nucleic DNA values of the carcinoma cells. It may thus be possible to distinguish between benign and malignant tumors of some tissues by a small series of nucleic measurements. If confirmed such a technique may become a valuable diagnostic tool. In experimental tumors the DNA value of the nuclei was correlated and equated with chromosome number and the possession of abnormal chromosome complements by malignant cells. Direct chromosome counts on fresh tissues obtained at operation gave a value identical with that calculated from the measured DNA value.

Repeated Doses of Poliomyelitis Vaccine.—Perkins and co-workers (*Brit. M. J.* 1:680, 1959) showed that the maternal antibody still present in 4-month-old infants inhibits their response to type 1 poliomyelitis vaccine. Satisfactory response will be obtained in all infants only when maternal antibody has fallen to noninhibitory levels, which is after the infant is 6 months old. They therefore investigated the responses to poliomyelitis vaccine given as a primary course of immunization (*Brit. M. J.* 2:530, 1959). Sixteen infants in each of these two age groups were given three doses of 1 ml. of vaccine intramuscularly, each at an interval of a week. Postimmunization blood samples were taken four weeks after the second dose, and two to three weeks later.

The responses of infants in both age groups to two doses of vaccine were good to type 2 and type 3 virus, all the infants responding, but those to type 1 were not so satisfactory; 20% of the 6-month-old infants and 43% of the 9-month-old infants failed to show a rise in antibody level. The responses after three doses were much more satisfactory, all infants giving higher antibody levels to all types than after two doses. The 6-month-old infants responded better to type 1 virus than did the 9-month-old infants, and this difference was most pronounced after the third dose. This was probably due to the difference in antigenic activity of type 1 virus in the two types of vaccine used. Only vaccines highly potent in the type 1 component should be used for immunizing infants. Three doses, given at monthly intervals, should constitute the primary course at this age.

Peripheral Vascular Disease Treated by Placental Implants.—Falconer and Gunn (*Brit. M. J.* 2:538, 1959) conducted a controlled trial on the effect of placental implants for the relief of symptoms in patients with peripheral vascular disease. The investigation was prompted by the reports of continental workers who claimed that placental extracts promoted the healing of wounds and ulcers. A series of 39 patients with severe intermittent claudication was divided by random selection into five groups, which were respectively treated with an implant of (1) placenta; (2) penicillin and saline solution to act as a control for the trauma of the incision; (3) the fluid in which the placenta was incubated, which was virtually a saline placental extract; (4) human protein to excite a foreign body reaction; and (5) 150 mg. of ethinyl estradiol. Under aseptic conditions a number of 1-cm. cubes of the cotyledon surface of freshly delivered placentas were excised and incubated at 4 C for five days with one mega unit of penicillin in 4 ml. of normal saline solution. Three 1-cm. cubes were then implanted subcutaneously in the thigh of the maximally affected limb. The patients of the control series received the implants or extracts previously described.

The results were assessed by determining before and after treatment the walking distance required to produce claudication, the venous filling time, the response to reflex heating, skin temperature, oscillometric readings, and the subjective feelings of the patient. Of those who received placental implants nearly 70%, claimed to be benefited for varying periods. There was an increase in exercise tolerance, a rise in skin temperature, and an improvement in the reflex heating response, but no change in the oscillometric readings. The control patients showed no subjective or objective improvement, except those receiving ethinyl estradiol, some of whom showed improvement for a short time. The authors believe that these placental implants have a place in the treatment of peripheral vascular disease. They ascribed the effect to hormones in the placenta, possibly estrogens, since ethinyl estradiol also appeared to have some beneficial action.

CORRESPONDENCE

NAMES OF NEW DRUGS

To the Editor:—The matter of names of new drugs continues to raise problems. For commercial protection, it is necessary for a drug manufacturer to trademark a name for a new drug. Such a name is usually made as short and as easy to remember as possible in order to maintain commercial advantage through use of the trade name, even after patent rights to the drug itself may have expired. On the other hand, it is against the dignity, prestige, and best interests of scientists and members of the health professions to use trade names of drugs in scientific and professional communications. There is no point in scientists or professional men becoming advertising agents for commercial concerns. As a consequence, generic names which may be publicly used without any fear of involving the legal aspects of trade names must also be provided.

In view of the increasing flamboyance of commercial advertising for drugs, even in the best professional journals, it is particularly important that professional men and scientists themselves attempt to hold the persuaders of Madison Avenue within reasonable bounds. This can be done editorially by suggesting more restrained drug advertising and especially by requesting more scientific data in the advertisements. It would help if we could get away a bit from our devotion to the psychology of persuasion, in business affairs, to the more farsighted viewpoint associated with the psychology of responsibility. It is still the responsibility of management in drug manufacturing to maintain the dignity of drug advertising.

A situation in which all scientists and professional workers would use only the generic names of drugs in scientific and professional communications, with perhaps merely a footnote to indicate the trade name for identification purposes, would be particularly helpful. The editors of scientific and professional periodicals could help by insisting on the exclusive use of generic names in all scientific and professional communications, with full disclosure of the chemical constitution of new drugs and data on physical and chemical properties, not only for purposes of identification but also for practical information. The Conference of Biological Editors is planning to consider this matter. This important group is developing a style manual which, it is hoped, may be followed by editors of scientific and professional journals.

Meanwhile, the American Medical Association could well afford to take the lead again in trying to exercise some sort of effective control over the developing abuse of drug advertising. This formerly was a function of its Council on Drugs. This matter could again be delegated to the Council on Drugs, by giving it authority to prevent the use of any advertisement of a drug which does not conform to simple decency and which fails to give specific information about the chemical composition of the drug, with the generic name and with such scientific data as may be useful to physicians in deciding whether or not to use the drug clinically. The better drug manufacturers will probably initiate steps themselves to bring about some measure of control over the insidious growth of over-persuasive drug advertising.

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CINCHONA BARK AND LOUIS XIV

To the Editor:—In the column "Medical Beliefs of Yesterday" in The Journal, Sept. 5, page 250, it is stated that Louis XIV of France was treated with quinine. This is not strictly true, in that quinine was not extracted from cinchona bark by Pelletier and Caventan in France until 1820, whereas Louis XIV was born in 1639 and died in 1715. The bark of the tree was called Jesuit bark in 1535. It was used as a drug in 1633, and it was given to the wife of the Viceroy of Peru in 1638. His family name was Cinchona or Chichona and the bark thereafter took its name from this family. The bark was introduced into France in 1649.

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PEPTIC ULCERS IN CHILDREN

To the Editor:—I am establishing a registry of children who have peptic ulcers. I believe that all physicians who are working in this field and who are interested in this problem should have some place to correlate their knowledge. I would appreciate it if anyone who knows of child patients with peptic ulcer, diagnosed either post mortem or roentgenographically, would send the pertinent data to me. I will circulate a semiannual report to everyone who contributes material to the register.

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THE LEISURE CORNER

MOBILES—A NEWER ART FORM

Contemporary artists and sculptors have experimented widely with new forms, compositions, and materials. A most interesting adaptation of movement occurs in the work of sculptors such as Alexander Calder, an American, who in 1930 introduced the use of mobiles. These sculptures are shapes made of wire and sheets of metal that are suspended in the air. Mobiles are linked together and balanced so that they will move and form a related composition when they are pushed by air currents.

A mobile is created for the sake of movement. Movement is unplanned, and it is the particular way in which it moves that captures the spectator's attention. Since mobiles comprise one of the newer art forms there is very little formal tradition or history behind their evolution, other than the fact that they were introduced about three decades ago. Mobiles are three-dimensional and artists everywhere refer to them as moving sculpture. When painted, they possess a quality similar to that of an abstract painting wherein all the pieces are cut out.

One of the fascinating aspects of mobiles is that, after they have been constructed and suspended in the air, they turn and present many combinations of form simultaneously. The outside and the inside of a mobile can be seen at the same time. Light, space, and form enter in equal balance as they are incorporated in the basic design. The space in which a mobile moves is as important as the mobile itself. A mobile is not supposed to just hang in the air, moving stiffly as a weathervane or a fixed windmill in a static and fixed manner. The secret of a well-constructed mobile lies in its ability to have a life of its own, being so constructed as to possess purposeful forms pointing in a variety of directions so that the observer will follow its graceful contour and rhythm. All the elements of motion can be controlled by the maker of the mobile, who will impart to each mobile a special character and personality—dreamy, solemn, or witty.

After a mobile is constructed, it should be hung as part of the decoration of a room in a space that will provide unrestricted movement. The center of a room is not necessarily the most desirable location. To be seen and best appreciated, a mobile is hung at eye level or a little higher, generally from the ceiling. Among the more desirable locations are the side of a wide door, an arch, an opening between rooms, in a bay window, or in a main entrance hall or foyer.

A cardinal question arising in the mind of a novitiate mobile-maker is how to balance the entire composition. If one keeps in mind that a mobile is not a machine for defying gravity or solving problems in physics, it will soon be realized that balance can be obtained by the artistic use of color, form,
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a mobile—motion, balance, and form.

The proper use of color is important in the design of a mobile, for color not only makes the mobile more attractive but in a subtle fashion achieves the desired balance. If both sections of cardboard in a two-piece mobile have the same neutral color, paint one of the sides of one section red. You will then notice that the red side becomes a focal point, and the other side seems to revolve around it as the mobile turns.

One of the attractive features of becoming a mobile hobbyist is the fact that mobiles are inexpensive and require only simple tools for their construction. To begin with, many of the objects required are usually found in one's home, for example, cardboard, sheet metal, wire, and thread. Later, as one becomes more proficient in the construction of mobiles, the main ingredients required are ample doses of ingenuity, imagination, and skill. Of course, these elements bring other products into play, and before you know it you will be experimenting with and utilizing wood, plaster of paris, plastic, glass, and paint.

When searching for ideas to be incorporated in mobile designs, one has to observe various environments. Abstract paintings in art museums have assisted many mobile hobbyists by suggesting interesting patterns and designs. Rectangular, horizontal, and vertical shapes will complement similarly designed spaces. Free forms—not necessarily geometric figures—are more adaptable and pleasing when the space occupied by the entire mobile is itself a free form. When working with free forms it is a good rule to arrange them in asymmetrical combinations, horizontal and diagonal, so that they will appear very much like the leaves of a branch of a tree. A well-constructed mobile should always appear to be floating or moving through the air, never hanging stiffly in space.

Many doctors, especially pediatricians, have placed mobiles in their offices. These seem to relax their young patients as they await their turn for examination. The eye-catching mobiles usually contain materials young children are familiar with—trinkets, colored papers in a variety of fantastic shapes, small boxes, jewelry, decorative accessories, all balanced on wires. Movement always affords a great deal of pleasure to children, and their visit to the doctor's office becomes an agreeable experience as a result of watching mobiles.

of the illness. In one of the 2 patients an anemic state caused by gastrointestinal bleeding was recognized early, and blood transfusion replacement therapy was started immediately. The provision of essential nutrition to the anoxic myocardium probably enabled the patient to recover from the acute injury. The other patient died of myocardial infarction several days after her gastrointestinal bleeding had been well controlled and her hematocrit stabilized. The fatal myocardial infarction could have been prevented if the diagnosis of gastrointestinal hemorrhage had been made earlier and subsequent blood replacement given sooner.

The principal causes of cardiac involvement in extensive gastrointestinal hemorrhage are the shock and acute anemia that accompany this process. Acute anemia by itself, without any drop in systemic blood pressure, is a treacherous enough situation, causing a decrease in the ability of the myocardium to meet its nutritional needs. Active bleeding causes a fall in cardiac output in the presence of tachycardia. Only after the phase of active bleeding has stopped does the anemic individual respond to the situation with an increase in cardiac output, provided that the myocardium is healthy enough to respond to the need.

Since anemia and shock are the principal precipitating causes of myocardial necrosis in hemorrhage, the correction of these 2 factors is the cornerstone of therapy. Under no circumstances should blood or pressor agents, such as levarterenol bitartrate, be withheld in the gastrointestinal bleeder when they are indicated. Circulatory stabilization will usually occur after rapid infusion of 1,000 or 1,500 cc. of whole blood, and blood may be given more slowly after this to regain hematocrit. If congestive heart failure is impending, the blood must be given slowly and the blood pressure maintained by pressor amines administered intravenously simultaneously. If circulatory stabilization does not occur after administration of 2,500 cc. of blood, it may be assumed that bleeding is continuing and that immediate operation is required.

Throughout the period of active bleeding the clinician must be aware of the cardiac status of the patient. Arrhythmias should be detected early, and specific drug therapy should be instituted. Electrocardiographic studies should be frequent; if myocardial infarction or coronary insufficiency occur, nonvital procedures, such as intubation and x-rays, should be avoided. Frequent observation to detect the early signs of congestive heart failure should be performed. If such signs occur, digitalis is administered rapidly. Cardiac studies should be as frequent as hematocrit and blood pressure determinations in these patients. Intravenous therapy with such a pressor amine as levarterenol should be used promptly when signs of hypotension are detected. It is suggested that a urinary catheter be inserted and the flow of urine in cubic centimeters per minute be measured at the same time as levarterenol is administered. The flow rate of urine in half a cubic centimeter per minute suggests a satisfactory response to pressor amine therapy, correlating well with the rise in systolic blood pressure and the widening of the pulse pressure to 20 mm. Hg.

Hypoplasia of the Pulmonary Arteries. J. R. Belcher, L. Capel, J. N. Pattinson and J. Smart. Brit. J. Dis. Chest 53:253-262 (July) 1959 [London].

The authors report on 12 men, between the ages of 28 and 58 years, and a 41-year-old woman with hypoplasia of the pulmonary arteries. The condition was discovered either on a routine chest roentgenogram showing increased radiolucency of one lung or of one or two of its lobes, due to this decrease in vascularity, or after the occurrence of such symptoms as dyspnea, bronchitis, and hemoptysis, for which the patients were referred to the London Chest Hospital. Of the 13 patients, a lobar artery was affected in 9, and the whole pulmonary artery on one side in 4. Bronchography and angiography were carried out in 11 patients, and bronchospirometry in 9. In addition to increased radiolucency of the whole or part of one lung, the chest roentgenograms showed decrease in size of the affected segment and great reduction in size of the pulmonary arteries. Angiography showed a great reduction in the size and number of the pulmonary arteries and a diminished circulation rate in the affected area. The angiographic appearances differed from those seen in emphysema in that the affected pulmonary artery was often small. In 2 of the 11 patients the bronchogram was normal; in the other 9 patients, a prominent reduction in size by more than 50% was seen, which differed from the abnormality of typical bronchiectasis. Bronchospirometry showed that the oxygen uptake was reduced considerably more than the ventilation on the affected side.

It is thought that hypoplasia of the pulmonary arteries may be congenital in origin or that it may be acquired during the growing period. Although the abnormal lobe or lung in itself causes no symptoms, the respiratory reserve is diminished, for the affected area takes up little oxygen. Hypoplasia of the pulmonary arteries thus may aggravate breathlessness due to disease in the unaffected lung. Whatever the cause of the lesion, the presence of a hypoplastic pulmonary artery is of practical importance. The onset of inflammatory or neoplastic processes in the only functioning lung is of much graver import than in the average patient and requires prompt treatment. Coexisting bronchiectasis can be treated on its merits, bearing in mind that one area of lung is almost functionless because of the arterial hypoplasia. If there is effort intolerance (the patient is unable to maintain normal walking pace) and severe trapping in the abnormal lung (which was present in each of the 4 patients with the whole of the right or left pulmonary artery affected), then pneumonectomy may help. This was performed on 2 patients, with great improvement in one, and slight improvement in the other. In neither patient was there any significant change in the spirometric findings after pneumonectomy. This reflected the severe ventilatory defect of the removed lung. The presence of hypoplasia of the pulmonary artery should be suspected whenever a lobe or lung shows increased radiolucency and diminished size. A close study of the vascular pattern on the chest roentgenogram will usually establish the diagnosis. Angiography may be helpful in doubtful cases.

Tuberculoid Granuloma in the Stomach. N. G. Kock. Nord. med. 62:1036-1039 (July 9) 1959 (In Swedish) [Stockholm].

Tuberculoid granulomas without necrosis have been seen in many organs. The first description of changes typical of sarcoidosis in the stomach was given by Schaumann in 1936. Tuberculoid granulomas are now regarded as an unspecific tissue reaction to a number of different agents. Kock found reports of 24 cases in the literature and describes 4 additional cases. The first of these fulfills the requirements for classification as sarcoidosis; tuberculoid granulomas without necrosis were found in 2 localizations—in the stomach mucosa and in a lymph node at the lesser curvature—also in lymph nodes from the axilla. Of the other 3 cases, all with peptic ulcers, the first case had tuberculoid granulomas in the stomach mucosa, and the second, in lymph nodes at the lesser curvature; in the third instance tuberculoid granulomas were found at the bottom of the ulcer and in a lymph node at the lesser curvature. The lesions are regarded as an unspecific reaction in connection with the ulcers.

Clinical Investigations on the "Rheumatoid Factor." M. Giordano, M. Ara and E. Drammis. Riforma med. 73:783-788 (July 11) 1959 (In Italian) [Naples].

The authors examined the so-called R. A. test, a remodification of the latex fixation test of Singer and Plotz which had originally been modified by Rheims and co-workers, in 113 patients with certain types of rheumatic disease and in 188 patients with nonrheumatic disease. The Waaler-Rose test (or W. R. test), as modified by Svartz and Schlossmann, was given to all patients with rheumatoid arthritis and to most patients who had not had rheumatoid arthritis but who showed positive or doubtful response to the R. A. test. Of 30 patients with primary chronic polyarthritis, the R. A. test finding was positive in 29 (96.7%), and the W. R. test was positive in 21 (70%). The serum of the only patient who had a negative R. A. result yielded a doubtful result with the W. R. test. Both A. R. and W. R. test findings were positive in the only patient who had rheumatoid arthritis associated with psoriasis. Two of 40 patients with rheumatic fever had positive R. A. test findings in a dilution of 1:16. The serum of 2 out of 3 patients with ankylosing spondylitis gave negative results with both the R. A. and the W. R. test. Findings with the R. A. test in dilution of 1:40 were positive in 6 (15%) out of 40 patients with arthrosis accompanied by pain. Of 133 diabetic patients, findings with the R. A. test in dilution of 1:40 were positive in 19 (14.2%). Positive results with the R. A. test were obtained in 4 out of 5 patients with Addison's disease. Of 8 patients with pulmonary tuberculosis and pleurisy, 2 gave positive R. A. results. The authors believe that the R. A. test is a useful method for the diagnosis of primary chronic polyarthritis; it is a slightly more sensitive and a much simpler procedure than the W. R. test.

The Prevalence of Pneumococcal Types and the Continuing Importance of Pneumococcal Infection. R. Austrian. Am. J. M. Sc. 238:133-139 (Aug.) 1959 [Philadelphia].

Data accumulated from 1952 to 1957, after the reintroduction of pneumococcic typing as a routine laboratory procedure in the New York area, in which this study was conducted, indicate that the pneumococcus is still an important cause of disease in the human respiratory tract and that there has been relatively little change in the distribution of the pneumococcic types responsible for most of the infections in man. The principal exception to this latter statement is the rarity, in the 6 years for which figures are available, of infection caused by pneumococcus, type 2. Variations in the incidence of infection due to this organism have been noted in the past.

Pneumococci were recovered from 1,322 patients admitted to a general medical ward service. About two-thirds of these patients had pneumonia. Classification of the strains isolated showed that 48.8% were included in capsular types 1 to 8, inclusive, and that two-thirds of 209 pneumococcic bacteremias were caused by organisms of these same capsular types. The course of infection has obviously been altered by the use of antibiotics in its treatment. Pneumococcic pneumonia treated soon after onset with highly effective modern drugs may be limited to a single pulmonary segment instead of progressing throughout an entire lobe or beyond it. The incidence of extrapulmonary complications has also been strikingly reduced. Nevertheless, patients arriving at the hospital in the advanced stages of pneumococcic infection continue to present many of the manifestations noted before effective antibacterial therapy became available and to succumb to the disease. In 1957, 5 patients with pneumonia and bacteremia and 3 with meningitis died.

It is a paradoxical fact that, since the advent of antibiotics for the treatment of pneumonia, laboratory techniques for the isolation and identification of pneumococci have been largely abandoned, probably for reasons of economy. These techniques are among the most precise and efficient in the field of bacteriology, and until they are restored and until capsular typing serum, now no longer commercially obtainable, can be made available again, mistaken ideas about the etiology of pneumonia will undoubtedly persist, and misdiagnosed "virus" pneumonia will continue to respond to treatment with antibiotics.

The Articular Manifestations of Chronic Ulcerative Colitis: An Analysis of 555 Cases. L. Fernandez-Herlihy. New England J. Med. 261:259-263 (Aug. 6) 1959 [Boston].

The records of 555 patients with chronic ulcerative colitis, seen at the Lahey Clinic from 1926 to 1955, were examined for references to articular manifestations. The purpose of this examination was to attempt to classify the manifestations found, to estimate their frequency, and to correlate them with the activity of the colitis. The general frequency of articular manifestations in these patients was found to be 17%. Rheumatoid spondylitis came first in order of frequency, followed by arthralgias, rheumatoid arthritis, erythema nodosum, and "acute toxic arthritis." The first 4 of these types are readily identifiable clinically, but the 5th does not fit under the heading of any of the recognized arthritides. This is the type that follows the colitis most closely and is relieved without sequelae by cure of the colitis. Its clinical characteristics are such as to suggest its temporary inclusion under the term "acute toxic arthritis." This term is obviously unsatisfactory, but until more is known about the arthritides in general and rheumatoid arthritis in particular, it seems to provide a useful classification.

An interesting feature of acute toxic arthritis, apart from its parallelism with the colitis, was the fact that only the large joints were involved. Five of the 10 patients whose condition placed them in this classification had acute polyarthritis sparing the small joints of the hands and feet. The remaining 5 had bouts of acute arthritis limited to a maximum of 3 joints, the knees, ankles, elbows, and wrists being the areas involved in that order of frequency. All 10 of these patients were subjected to colectomy, and the arthritis was cured in all cases, so that colectomy appears to be indicated in patients with acute toxic arthritis. None of the other 4 types of arthritis in itself constitutes an indication for colectomy. The relatively high frequency of rheumatoid spondylitis in patients with chronic ulcerative colitis suggests that a careful search for this condition should be made in all patients with chronic ulcerative colitis associated with back pain or peripheral joint symptoms.

Disseminated Coccidioidomycosis. H. F. Stein. Dis. Chest 36:136-145 (Aug.) 1959 [Chicago].

Dissemination follows failure of the body to "focalize" coccidioidomycosis at its primary site in the lungs. It is an endogenous reinfection and is manifested shortly after the primary infection of which it is a continuation. Coccidioidal pulmonary cavitation, however, seems to confer immunity against dissemination. When dissemination does occur, it involves every body tissue with the exception of the intestinal tract. Of the associated conditions, lymphadenitis and osteitis are common and may produce chronically draining abscesses in the neck, mediastinum, extremities, and other body regions. Metastatic abscesses are commonly seen in the liver, kidney, spleen, gonads, adrenals, and brain. Pulmonary consolidation may extend, resulting in abscesses and empyema. Myocarditis and pericarditis may develop. Meningitis may run an acute or chronic course. Clinically, dissemination of coccidioidomycosis is manifested by an exacerbation of the illness, associated with persistent spiking fever, loss of weight, increasing weakness and toxicity, and evidence of systemic spread. Temporary spontaneous remissions are not at all rare, but in the long run the disease has always proved fatal.

Many therapeutic agents have been tested unsuccessfully in the treatment of disseminated coccidioidomycosis. The newest available agent is amphotericin B (Fungizone). This antibiotic is formed by a hitherto unidentified species of Streptomyces isolated from a soil sample obtained at Tembladora, on the Orinoco River in South America. It is biologically standardized at a rate of 1,000 units per milligram. Fungizone, orally and intravenously, has been given to a small number of patients with various manifestations of disseminated coccidioidomycosis. In all these patients skin and bone lesions have healed. The usual oral dosage is 3 or 4 Gm. daily in 4 to 6 divided doses, but larger doses may be given in advanced cases. Intravenously, an initial dose of 0.25 mg. per kilogram should be given over a period of about 6 hours. This dose should be increased to a daily optimum of 1 mg., depending on the severity of the infection and the patient's tolerance. The initial intravenous administration of Fungizone is usually associated with a febrile response, often accompanied by chills. These reactions diminish with successive infusions and can be relieved by aspirin and antihistamines. It thus appears that Fungizone is a hopeful new agent in the treatment of disseminated coccidioidomycosis. The author describes the history of 4 patients with disseminated coccidioidomycosis, who were observed at the Tucson (Ariz.) Veterans Administration Hospital.

Giant Ulcers of the Stomach. I. Cohn Jr., J. Sartin and P. Sudduth. Am. J. Gastroenterol. 32:121-135 (Aug.) 1959 [New York].

Current medical opinion favors the view that the incidence of cancer increases with the size of a gastric ulcer. In order to find out whether this view was correct, the authors studied 48 selected patients with gastric ulcer, in whom the pathological report stated that the diameter of the ulcer was 2.5 cm. or more. Forty of these were benign "giant" gastric ulcers. The age distribution (from 20 to 80 years) was as expected for chronic ulcer disease, with the greatest incidence in the 5th decade. The size of the ulcer and the reaction surrounding it suggest a chronicity of disease, which is borne out by the history of ulcer symptoms. More than half of the patients had had symptoms for 1 year or longer, and almost one-third had had symptoms for more than 5 years; 10 patients had had symptoms for from 10 to 34 years. The presenting symptoms were not significantly different from those of patients with peptic ulcers in general. Twenty-seven patients had had previous treatment for gastrointestinal disease, including 3 with previous perforation. Physical findings were generally of no specific help in those admitted with either an acute perforation or a massive bleeding. An abdominal mass was palpated in 4 patients, each of whom was thought to have carcinoma, although each was found to have a benign ulcer.

There were also no differentiating facts in this series, connected with age, sex, color, roentgenologic diagnosis, gastroscopic study, gastric analysis, location of ulcer, or occurrence of complications, which could have served to distinguish the giant ulcers from other smaller gastric ulcers. The failure of all the usual diagnostic studies to provide a definitive diagnosis emphasized the importance of histological examination of the specimen. No characteristic clinical picture of the large gastric ulcer has emerged from this study, but one fact stands out, i. e., that carcinoma developed in only 33% of even the largest ulcers with a diameter of 4 cm. or more, which is in contradiction to the generally accepted concept of a greater incidence of malignancy in large gastric ulcers. The review of the literature showed that in 553 patients with gastric ulcer of over 2.5 cm. in diameter the ulcer was benign in 72% and that in 136 patients with ulcer larger than 4 cm. in diameter only 37% of the ulcers were malignant. It is emphasized that large gastric ulcers do not respond to medical treatment. Conservative surgical management gives more satisfactory results and should be considered the treatment of choice in patients with large gastric ulcers.

The Long-Term Prognosis Following Myocardial Infarction: Clinical Control of 180 Patients After 1 to 18 Years. P. Bregani, A. Selvini and V. Pavesi. Minerva med. 50:2343-2348 (July 21) 1959 (In Italian) [Turin, Italy].

It is estimated that cardiovascular disease is the cause of 2 out of every 3 deaths that occur in Italy. Myocardial infarction is still a very much feared disease, and most of the patients who recover from it live in constant fear of a relapse; some of them fail to return to active life and consider themselves invalids. A clinical and electrocardiographic study, which the authors made from 8 months to 18 years after the acute episode among 180 persons who had suffered from myocardial infarction, however, does not warrant such a pessimistic prognosis. One hundred fifty-two of the patients in this series were men and 28 were women, with an age range from 30 to 80 years. The infarct was severe in 67 instances (37%) and of first degree (according to Russet and Zohman's classification) in 113 (62%). Fifty-nine patients were treated at home, and 121 at a hospital where they remained for an average period of 43 days. Ninety patients received anticoagulants for an average of 32 days; the others did not. The infarct was located anteriorly in 73 cases (40%), posteriorly in 63 (35%), and anterolaterally in 27 (15%). Twenty-two patients (12.2%) died during the acute phase of the infarct (the first 43 days from its occurrence). No patient who died during the first 24 hours after the infarct was included in the series.

There were 21 deaths among 127 patients who were followed up and examined after recovery from the infarct. Altogether, death, immediate or late, occurred in 28.7% of the patients. Of the 21 late deaths, 9 occurred in the first year after the infarction and 8 in the second year. Most of the patients who survived (73.5%) were in good health; 46.2% of them had returned to their normal activities as before the infarction; 27.3%, though in good health, had cut down on their work schedule; and 26.5% were in poor health, suffering from various cardiocirculatory disturbances, mainly angina pectoris (12.5%) and cardiocirculatory decompensation (11%). A relapse occurred during the acute phase of the infarction in 9 (5%) of the 180 patients of the series and in 21 of the 127 who survived. Among the latter, the relapse occurred mainly within the first 2 years after the acute phase—in 10 patients in the first year and in 7 in the second. Thromboembolic complications were observed in 6 patients.

Among the patients with severe infarction who were treated with anticoagulants during the acute phase of the disease, late observations showed an apparently complete clinical recovery in 48% and a persistence of various cardiocirculatory disturbances in 32%; among the patients of the same group who were not treated with anticoagulants, 38% had recovered and 44% showed cardiocirculatory disturbances. The electrocardiogram showed a further favorable evolution, with partial or even complete regression of alterations in 69% of the patients who had returned to normal health. It remained stationary or showed changes for the worse in 70% of the patients in whom cardiocirculatory disturbances had persisted or had occurred subsequently.

Progressive Systemic Sclerosis or Scleroderma: Experience with 67 Cases. A. Gonzalez S. Rev. méd. Chile 87:498-616 (July) 1959 (In Spanish) [Santiago].

The diagnostic and therapeutic problems in 67 cases of progressive systemic sclerosis, observed in the adult service departments of 2 hospitals in Chile, are discussed. Only 6 of the patients were men. The ages of the majority were between 21 and 60 years. The course of scleroderma varies greatly, as shown in this series by the variation in the time interval between the first symptoms and the establishment of the diagnosis. It varied between 4 months and 23 years, although in most cases (79%) this interval was 1 to 10 years. The most frequent initial symptoms, and the most indicative of the disease, were Raynaud's phenomenon in 36 patients (55%) and arthralgia in 16 (25%). The various signs and symptoms were classified in 3 categories: general, localized, and parenchymatous or visceral. The most frequent in the general category were hardening of the skin (not an initial sign), pigmentation, and Raynaud's phenomenon in the proportions, respectively, of 85, 78.5, and 73%. As localized symptoms, involvement of the bones of the hand and subungual necrosis were found, respectively, in 74 and 46% of the patients. The most frequent visceral involvements were bronchopulmonary (45%), cardiovascular (43%), and esophageal (34%).

Several therapeutic procedures were used, such as glandular extracts, ether given intravenously, and Novocain, but without any definite results. The administration of steroids was the most successful therapy for relieving the symptoms. In one patient of this series, who was hospitalized in very serious condition and to whom prednisone in initial doses of 40 mg. daily (later reduced to 10 mg.) was administered, the results were dramatic. After a period of 2 years this patient was leading a normal life under a maintenance dose of 10 mg. daily. The results of the administration of corticoids (cortisone and prednisone) are presented in relation to 17 patients. A combined therapy with cortisone and prednisone was given in 2 cases; cortisone only was given to 1 patient, and prednisone only to 13 patients. The results were excellent in 1 patient, very good in 7, good in 6, fair in 1, and unsuccessful in 2 (one patient had to interrupt the treatment due to intolerance symptoms, and the other died). The author considers corticoid therapy as the most effective means of halting the course of progressive systemic sclerosis, improving the general condition and the visceral involvement, and relieving the pain. However, he cautions against the danger of side-effects, which may cause interruption of the treatment.

Chronic Myeloid Leukemia: A Study of 86 Patients. C. K. Hambly and T. I. Robertson. M. J. Australia 2:75-84 (July 18) 1959 [Sydney].

The average length of survival of patients with chronic myeloid leukemia is known with reasonable certainty, but it is important to know the effect of treatment on the well-being of the patients during their remaining months. The authors approached this problem by reviewing the records of 86 patients with chronic myeloid leukemia, who were treated at Sydney Hospital between 1922 and 1958. The ages of the patients ranged from 10 to 80 years. A peak incidence of the disease occurred between the ages of 40 and 60 years, with a slight predominance in male patients. The prevalent symptoms presented by the patients were anemia, palpable abdominal swelling, pain, or loss of weight. Patients survived, on the average, 2 years from the time the first diagnosis was made, and their survival was little affected by sex, age, or duration of symptoms before the diagnosis. The survival periods with most forms of treatment were approximately the same, although patients who were treated with low voltage roentgen radiation, combined with the administration of arsenic or benzol, died sooner than those who had not received this therapy.

Preliminary blood transfusion for the severely anemic patient is considered important. Among various chemotherapeutic agents used in this series, Myleran seemed to be the treatment of choice in patients with chronic myeloid leukemia by the ease of its administration, and by the absence of dangerous and unpleasant side-effects, provided that the treatment is judiciously applied. The authors used deep roentgen-ray therapy only in patients with focal pressure symptoms and pronounced hepatosplenomegaly as a preliminary treatment to Myleran, depending on the patients' physical condition and response. Myleran was given orally in the fasting state as a single dose of from 4 to 6 mg. each morning of treatment, and maintenance dosage varied from 0.5 to 4 mg. per day. The aim was to reduce the number of leukocytes to approximately 10,000 per cubic millimeter. Treatment was then discontinued in some patients, and was resumed only when relapses occurred; other patients were given continuous maintenance treatment. The treatment brought about great improvement in general well-being and in capacity to work in almost all the patients. Most of the patients, at one time seriously incapacitated, remained reasonably well and were employed until close to death.

When Myleran ceased to be effective, other chemicals were of limited use, and death ensued rapidly, mostly because of acute leukemia often complicated by hemorrhage. Deep roentgen-ray therapy is not indicated and can be even harmful when this chemical resistance develops.

Sjögren's Syndrome: Report of a Fatal Case with Pulmonary and Renal Lesions. U. G. Bucher and L. Reid. Brit. J. Dis. Chest 53:237-252 (July) 1959 [London].

The authors report on a female patient with Sjögren's syndrome, whose death occurred from massive cerebral hemorrhage after a long illness at the age of 22 years. The syndrome was diagnosed at the age of 13 years, when the triad, keratoconjunctivitis sicca, xerostomia, and parotid swelling, had developed and was associated with joint pains and scoliosis. All treatment was unsuccessful, including several courses of antibiotic drugs which, although controlling the patient's repeated attacks of pneumonia, did not alter the fatal course of the disease. At autopsy, the lacrimal and salivary glands showed the characteristic atrophy of parenchyma with lymphatic infiltration. The mucous glands of the bronchi and esophagus showed a similar aspect. In the lungs a type of lesion not previously described was found, i. e., nodules of hyaline material, several centimeters in diameter, which were associated with arteritis, as well as smaller, probably earlier changes of exudative pneumonitis with giant-cell arteritis. Arterial changes were confined to the lungs and involved the smallest arterioles as well as larger vessels. The kidneys showed varying stages of glomerulitis and interstitial infiltration with plasma cells and lymphocytes.

These findings and those reported in the literature suggests that Sjögren's syndrome, besides being clinically a well-defined entity, has a recognizable pathological picture characterized by atrophy of the parenchyma of salivary and lacrimal glands and also of the bronchial wall and esophagus and its replacement by dense infiltration of lymphocytes and plasma cells. An early change in the glands is the irregularity or loss of the reticulin pattern; fibrosis is not a striking feature. These changes have been associated with vascular lesions sufficiently frequently to suggest that they play an important, if as yet undefined, part. The vascular changes may occur in only one organ and can be a necrotizing type of arteritis or a perivascular giant-cell arteritis with hyalin deposits as in this patient. The varied manifestations of the disease in this patient leave undecided whether Sjögren's syndrome is of a generalized nature, protean in its manifestations but the result of a particular and single cause, or whether there are a variety of causes which can give rise to the various changes which have become identified with the name.

Hemorrhagic Duodenitis in Myocardial Infarction. A. M. Katz. Ann. Int. Med. 51:212-218 (Aug.) 1959 [Lancaster, Pa.].

During the last 6 years the author observed "hemorrhagic duodenitis" at autopsy in 25 cases. This group included 18 men and 7 women, whose ages ranged from 37 to 78 years, with an average age of 57. Acute myocardial infarction was detected in 20 of the 25 patients; the causes of death in the remaining 5 were cerebrovascular accident with shock, brain tumor, pulmonary thrombosclerosis, possible penicillin reaction, and bacterial endocarditis with abscess of a papillary muscle. Although the majority of the patients died with a clinical picture of shock and left ventricular failure, 4 died suddenly, presumably of ventricular fibrillation or cardiac standstill. In one patient tarry stools and hematemesis were noted shortly after the onset of substernal pain and continued for 3 days, until death. No anatomic cause other than the duodenitis was found for the bleeding. Although the majority of the patients received anticoagulant therapy, there was no evidence of generalized bleeding. Thirteen of the 20 patients with acute myocardial infarction also had one or more old myocardial scars. Anatomically, there were 6 acute posterior infarctions, 10 anterior, 1 anterior and posterior, and 2 not specified; one patient had a fresh thrombus in the left coronary artery without gross or microscopic evidence of damaged myocardium.

The author points out that, although hemorrhagic duodenitis has been observed in association with extensive burns, injury to the central nervous system, tumor of the brain, and major operative procedures, its frequent concurrence with infarction of the heart has not been reported. He feels that the association of the duodenal and myocardial lesions is best accounted for by invoking a neurogenic vasomotor response, possibly a phase of the so-called alarm reaction. The duodenal hemorrhage may be responsible for some instances of abdominal pain in patients with myocardial infarction, and should be considered in the differential diagnosis of upper gastrointestinal bleeding in patients with arteriosclerotic heart disease.

Studies on Acute Rheumatic Fever in the Adult: II. The Rebound Phenomenon. S. K. Elster and E. Pader. Ann. Int. Med. 51:339-358 (Aug.) 1959 [Lancaster, Pa.].

The cases of acute rheumatic fever analyzed in this paper comprised 49 patients at the Mount Sinai Hospital, New York, who were studied in the period 1952-1957. They were followed carefully by daily physical examinations and frequent laboratory tests. Various therapeutic regimens were employed. During the period of lowering of drug dosage, and after complete withdrawal of drugs, clinical and laboratory examinations were intensified to detect evidence of the "rebound phenomenon." The rebound phenomenon was considered to have occurred if one or more of the following manifestations appeared, unassociated with other known causes, upon reduction or discontinuation of suppressive drug therapy: fever, elevation of the erythrocyte sedimentation rate, reappearance of C-reactive protein in the blood, arthralgias, arthritis, chest pain, electrocardiographic abnormalities, pericarditis, or congestive heart failure. When a rebound occurred, therapy was withheld for several days, and was reinstituted only when it became apparent that the rebound was not self-limited, or if the intensity of the rebound manifestations was severe. Such patients were then further observed, after withdrawal of drugs after retreatment, for the appearance of additional rebound states. Four of the 49 patients were discharged from the hospital while still receiving suppressive therapy, and no information is available concerning their response after cessation of treatment. Two patients died while in the hospital. The rebound phenomenon was observed in 22 of the remaining 43 patients, and 21 patients remained free from it. Fourteen of the 22 patients had 1-rebound, 7 had 2 rebounds, and 1 had 4 rebounds.

Fever, tachycardia, and arthralgias were the commonest clinical manifestations, with arthritis and pericarditis occurring less frequently. Elevation of the erythrocyte sedimentation rate, reappearance of C-reactive protein, and, less commonly, the appearance of electrocardiographic changes were the laboratory findings. Factors affecting the incidence of the rebound were reviewed, and no consistent relationship was noted in regard to duration of illness prior to therapy, duration of therapy, or mode of withdrawal of drugs. It is suggested that the highest incidence of the rebound was in the group receiving large doses of adrenocortical hormones, and that abrupt withdrawal of these drugs provoked the appearance of the rebound more commonly than did abrupt withdrawal of salicylates. The manifestations of the rebound phenomenon responded quickly to reinstitution of therapy. It is suggested that the rebound phenomenon is an indication of persistent rheumatic activity and, as such, requires further therapy.

Mechanisms, Diagnosis and Treatment of Hypertension of Renal Vascular Origin. I. H. Page, H. P. Dustan and E. F. Poutasse. Ann. Int. Med. 51:196-211 (Aug.) 1959 [Lancaster, Pa.].

The mechanisms of the relationship of the kidneys to hypertension have not been completely explained, since control of arterial pressure depends upon many mechanisms. The authors are concerned with only a few aspects of the multiple vascular controls, in which the kidneys are directly involved. Hypertension of experimental renal origin and human renal hypertension are probably initiated by a change in character of the pulse wave in the renal arteries, followed by release of renin. It is known that the renal proteolytic enzyme, renin, splits a peptide from a protein substrate that is synthesized by the liver. This first peptide contains 10 amino acids. It is a decapeptide called angiotensin I, and it has little pharmacological activity. An enzyme in the blood, called "converting enzyme," splits histadylleucine off the decapeptide, leaving an 8-amino-acid peptide; this octapeptide is the active pressor agent, angiotensin. No method has been developed for the measurement of angiotensin which has proved sensitive enough to measure minute amounts. If angiotensin is a vital part of the mechanism of renal hypertension, then avenues are open to block its effects, and it is probable that a chemical will be found to block the action of angiotensin.

Primary renal hypertension in man may be due either to parenchymal disease or to renal artery lesions. The first group is well represented by cases of glomerulonephritis and pyelonephritis. If patients with hypertension are subjected to a through analysis, from 25 to 30% are found to have renal artery lesions. Intravenous and retrograde pyelography and aortography currently constitute the most important diagnostic methods. Measurement of split renal functions is a valuable indicator of renal disease but does not always differentiate unilateral and bilateral involvement. The composition of the urine is determined by the renal lesion, rather than by the cause of the hypertension. Renal hypertension is usually of moderate severity, as indicated by eyeground examination; it may occur in the very young, but often occurs in the age group when atherosclerosis is common.

In the research division and the department of urology of the Cleveland Clinic, the authors studied 89 patients with hypertension and renal artery disease. Fifty-nine of these patients were operated on, and 30 were treated medically. Thirty-eight were subjected to nephrectomy, 6 to segmental resection of the kidney, and 15 to vascular surgery. The responses to these forms of treatment were, on the whole, satisfactory. Thirty-one have shown normal blood pressure for from 2 months to 6 years, and it is expected that it will stay normal. Another 7, all over the age of 55 years, still show some residual systolic hypertension with normal diastolic pressure, which is not surprising in view of the marked arteriosclerosis in many of these patients. In 7 patients the blood pressure was reduced, and in 9 it was unchanged. Five deaths occurred in association with the operation. Six other patients died from 6 months to 3 years after operation as a result of progress of the vascular disease. When arterial pressure was unchanged as a result of operation, stroke was the usual cause of death, and myocardial infarction if blood pressure was lowered. There is still much to be learned about surgical techniques, and improvement in surgery will have to be balanced against constantly improving medical treatments. Since it is not known how rapidly renal arterial lesions advance, it will always be a guess as to the urgency of the need for surgical correction of these lesions. Surgery may be ill-advised if (1) the patient has extensive cerebral or coronary atherosclerosis; (2) renal function is severely depressed; (3) aortic aneurysms are present in both thorax and abdomen; (4) the patient is elderly; (5) renal function is not deteriorating, and hypertension is moderate in a middle-aged person; and (6) the experience of the surgeon is inadequate to the task.

Esophageal Moniliasis Treated with Amphotericin B. A. Stenderup, J. Bichel and K. B. Jensen. Ugesk. laeger 121:1124-1127 (July 16) 1959 (In Danish) [Copenhagen].

In 5 patients in poor general condition, with a malignant disease and unfavorable prognosis, esophageal moniliasis was diagnosed roentgenologically or by esophagoscopy. Treatment with amphotericin B gave good results, both objectively and subjectively, except in one case. It is important to be able to treat effectively a complicating fungous infection which can cause so much discomfort.

Case of Cryptococcosis (Torulosis). K. R. Eriksen, E. Jensen, E. Reske-Nielsen and others. Ugesk. laeger 121:1127-1131 (July 16) 1959 (In Danish) [Copenhagen].

Cryptococcus neoformans seems to be widely distributed in nature. Definite relation between the occurrence of the fungus in nature and cryptococcosis in man has not been established. Fully 300 cases of cryptococcosis have been reported in the literature (Littman and Zimmerman, 1956). The infection is most frequent between the ages of 40 and 60 years, and men are affected oftener than women. The portal of entry is apparently most often the lungs. The fungus spreads from the primary focus and can affect any organ. In most cases the infection is localized in the central nervous system, with symptoms of meningitis or cerebral disease. The prognosis is unfavorable. Treatment with a new antibiotic, amphotericin B, should be tried in all cases. Diagnosis is made by establishment of cryptococci by culture or by direct microscopy. In differential diagnosis, tuberculous meningitis is most important. A case from the Rigshospital is described. At autopsy, lymphogranulomatosis of Hodgkin's type was established, with infiltrations into the spleen, pancreas, omentum, spinal column, and tissue over the upper part of the sternum. Culture demonstrated disseminated infection with C. neoformans; on microscopic examination this fungous infection was also seen in the central nervous system, kidneys, and lungs. The case was regarded as a disseminated cryptococcosis with typical processes in the central nervous system, originated in a patient with Hodgkin's disease. Generalized infection with a Candida species and Staphylococcus aureus was also found. Such simultaneous generalized infection with cryptococci and Candida organisms is considered rare.

The Course and Prognosis of Histoplasmosis. H. Rubin, M. L. Furcolow, J. L. Yates and C. A. Brasher. Am. J. Med. 27:278-288 (Aug.) 1959 [New York].

A review of the laboratory records at the Kansas City Field Station of the U. S. Public Health Service revealed that 123 culturally proved cases of histoplasmosis had occurred during the past 12 years. The patients were classified into 3 groups according to the clinical type of the disease, which was chronic pulmonary in 90 patients, acute pulmonary in 8, and disseminated in 25. The 90 patients with chronic pulmonary histoplasmosis ranged in age from 26 to 79 years; 92% were men, and 8% were women. Chronic pulmonary histoplasmosis is characterized by cavities in the upper lobes, and by gradual progression of the disease over several years. The length of follow-up of these patients from the time of their first abnormal roentgenograms ranged from 2 months to 26 years; the average follow-up was 40 months. The disease was fatal in 16 of the 90 patients; death was due to the pulmonary disease in 9, to pulmonary surgery in 4, to myocardial infarction in 2, and to bronchogenic carcinoma in 1. The average duration of illness in the patients who died was 69 months. The majority of these 90 patients spent years in tuberculosis sanatoriums despite the absence of tubercle bacilli in their sputums. More than half of these patients also had negative reactions to tuberculin skin tests. Twelve per cent of these patients were proved to have concomitant pulmonary tuberculosis, which was probably due to infection as a result of exposure to the disease after their admission to the sanatorium.

Twenty-five patients (18 male and 7 female) had disseminated histoplasmosis; their ages ranged from less than 6 months to 79 years. Included in this group were patients with seemingly isolated mucous membrane lesions. Such cases are usually fatal within one year, although occasionally a patient may survive. Nineteen of these 25 patients died as a result of their disease, making the overall mortality 76%. The duration of the disease in those who died ranged from 1 to 30 months. Three of the 6 living patients were treated with amphotericin B, and have been followed up for 1 month, 1 year, and 1 year respectively. The remaining 3 were not given any specific treatment, and are alive and well after follow-up periods of 7, 8, and 11 years respectively. Fourteen of the 25 patients gave positive reaction to the skin tests; 11 did not react to histoplasmin. This high percentage of negative reactions to the skin test may be a reflection of the clinical severity of the disease.

Eight patients (7 male and 1 female) had acute pulmonary histoplasmosis, which was the acute epidemic variety in 7. The clinical severity of this type of the disease correlated well with the time and intensity of exposure to the "point source" of infection, the most frequent being unused chicken coops or caves and damp shaded areas of soil. The duration of clinical illness ranged from 19 days to 3 months. All these patients are alive and well after follow-up periods averaging 3 years.

Cryptococcosis (Torulosis or European Blastomycosis): Review. N. J. Brandt. Ugesk. laeger 121: 1121-1123 (July 16) 1959 (In Danish) [Copenhagen].

Cryptococcosis designates a half-acute or chronic infectious disease due to the fungus cryptococcus neoformans, which is widely spread in nature in nonpathogenic form. About 500 cases of the disease have been reported in the literature. It occurs at all ages but most frequently in middle life. The respiratory tract is thought to be the portal of entry. C. neoformans can attack all organs, but it predominantly affects the lungs and the central nervous system. The course is usually chronic; spontaneous remissions seem to occur, but the condition can suddenly change to a disseminated fatal form. The meningeal form of cryptococcosis is far more serious than the pulmonary form. The first and dominating symptom is headache, violent and constant. Vomiting and dizziness occur, with anorexia and loss of weight. As the case advances, rigidity develops, and the patient becomes increasingly irritable, with confused mind, epileptiform spasms, hemiparesis and comatose condition, and fatal outcome. The course, as a rule, extends over months; in especially fulminant cases it may last for less than a month, and in more chronic cases for years. Diagnosis is made by direct microscopic examination and by culture from the cerebrospinal fluid. In the disseminated form metastatic foci are found in all organs. The results of therapy are difficult to evaluate because of the frequently prolonged course and spontaneous remissions. Good results have been achieved with a new agent, amphotericin B. Both clinical and pathoanatomic findings show that cryptococcosis can be difficult to distinguish from a number of diseases. It is often seen in combination with Hodgkin's disease, lymphosarcoma, leukemia, Boeck's sarcoid, and tuberculosis. Often earlier, apparently well-founded diagnoses must be revised after demonstration of C. neoformans. In every atypical case of the diseases mentioned, this fungus should be looked for.

SURGERY

Surgical Treatment of Atherosclerotic Occlusive Lesions in Patients with Cerebral Arterial Insufficiency. E. S. Crawford, M. E. De Bakey, W. S. Fields and others. Circulation 20:168-180 (Aug.) 1959 [New York].

Cerebral arterial insufficiency may often be caused by atheromatous occlusive lesions located in the extracranial portions of the arteries supplying the brain. Fortunately, these lesions are well localized, with the artery being relatively normal, both proximal and distal to the occlusion, particularly in the early stages of the disease. The well-localized lesion may be removed by endarterectomy, or, when the lesion is more extensive, the occlusion may be by-passed with a graft. The authors have employed this form of therapy in patients with cerebral arterial insufficiency. Arteriographic studies were performed in 174 consecutive patients with the clinical manifestations of ischemia of the brain or upper extremity. Extracranial arterial occlusion was demonstrated in 73 patients (42%). Operation was employed in the treatment of 63 of these patients. The remaining 10 patients are excluded from this study, because they had complete occlusion of the internal carotid artery of long duration, which extended well into the intracranial portions of the artery. Occlusion of the great vessels arising on the aortic arch was manifested clinically by symptoms of arterial insufficiency of both the cerebrum and the upper extremities and diminution or absence of pulses in the neck or arms. The precise location and extent of occlusion in patients with internal carotid and vertebral artery occlusions was evident only by arteriography.

A total of 115 extracranial arterial occlusive lesions existed in the 63 patients subjected to operation, 32 (50%) having multiple lesions. Eighty-eight of the 115 lesions were explored surgically, and circumstances favorable for restoration of circulation were found at exploration of 75 lesions, which were found to be segmental in nature with a normal extracranial segment, both proximal and distal to the obstruction. Employing endarterectomy in 37 well-localized lesions and graft bypass in 38 more extensive occlusions, circulation was restored in 72 arteries. Circulation was restored in all patients with lesions in the great vessels arising from the aortic arch, in 97% of those with operable lesions of the internal carotid artery, and in 60% of those with occlusions of the vertebral artery.

Severe cerebral arterial insufficiency, manifested by coma and extensive paralysis, was present before operation in 3 patients. Although circulation was restored in one or more of the occluded arteries, brain damage was persistent, and the patients' fatal terminal courses were unaltered. Death in 3 other cases was due to myocardial infarction in 2 and to hemorrhage in 1. The remaining 57 patients recovered, and circulation was restored in one or all of the occluded vessels in 47 patients. All patients with lesions of the great vessels arising from the aortic arch were completely relieved, and the majority of patients with lesions of the internal carotid and vertebral arteries were either relieved or significantly improved. These patients have been followed up for periods of more than 5 years, and the success achieved by operation has been well maintained.

The Present Status of Thymectomy in Myasthenia Gravis: A Review of Three Cases. H. H. Olson, N. M. Briggs and W. B. Spickard. Am. J. Surg. 98:196-201 (Aug.) 1959 [New York].

The authors report on 3 women, aged 21, 66, and 24 years, respectively, with myasthenia gravis, who were treated by surgical removal of the thymus. The second patient had supplemental irradiation therapy. The first patient no longer required neostigmine therapy after the operation except for an occasional tablet when she worked hard. She became pregnant 6 months later and had no difficulty during or after pregnancy. She now vorks hard caring for her family and does outside vork without difficulty. The result obtained in this atient is to be considered as near perfect. In the econd patient, thymectomy was definitely lifesavng. The patient would have died of the large hymic tumor without its surgical removal, as her nyasthenia was getting progressively worse. It has emained stationary ever since with some improvement. In the third patient, the thymectomy arrested the downhill course temporarily and perhaps prolonged the patient's life by several years. The effects of stress produced by the surgical intervention must also be considered in evaluation of marked but temporary postoperative improvements.

The results obtained in these 3 patients with myasthenia gravis treated by thymectomy tend to support the conclusions drawn by larger groups with a statistically significant series of cases. Most young women with myasthenia gravis of 2 or 3 years' duration and no evidence of thymic tumor should undergo exploration. Thymectomy is of doubtful value after 10 years' duration of symptoms. All patients with suspected tumors of the thymus without myasthenia gravis should undergo exploration, as well as those with concomitant myasthenia gravis, but only after careful evaluation. One should carefully balance the risk against the possible benefits. Thymectomy in male patients has not been completely evaluated but is considered to be of doubtful value. Irradiation therapy is of questionable value but is used in patients who are poor operative risks. Further studies on the physiological role of the thymus in myasthenia gravis and in normal conditions are essential to the successful treatment of the disease.

Current Concepts of Thymomas. R. W. Jamplis and R. D. Cressman. Am. J. Surg. 98:202-210 (Aug.) 1959 [New York].

The authors' review of the literature on thymomas shows that in the past confusion has reigned concerning the treatment, prognosis, and malignant potentialities of thymic tumors. This occurred mainly because there was no uniformity of opinion concerning the microscopic characteristics of the tumors. If one considers thymomas to be tumors which are composed always of two-cell types, namely, the epithelial cell and the classic thymocyte (lymphocyte), they fall into a very definite pathological and clinical entity. Thus, they can be distinguished readily on both these grounds from other small-cell tumors of the mediastinum, such as lymphoma; oat-cell bronchogenic carcinoma, teratoma, or germinoma. Thymomas rarely show embolic metastases but are potentially malignant by virtue of their capacity to invade vital mediastinal structures. Even when they do so, the usual histological criteria for malignancy are lacking. Therefore, it is essential that surgical intervention be radical, perhaps necessitating the excision and grafting of involved great vessels, as surgical extirpation is the only method of cure. Roentgenotherapy is palliative only but should be used in inoperable cases.

The association of thymomas, myasthenia gravis, agenesis of erythrocytes, and agammaglobulinemia remains an interesting and puzzling problem. That interrelationships exist between these entities seems irrefutable, but the exact mechanisms involved remain obscure. The authors believe that all thymomas, whether associated with myasthenia gravis or not, should be removed, because of their malignant capabilities. Whether or not to remove the thymus gland from patients with myasthenia gravis depends on the sex and age of the patient and the severity and duration of the disease. The best results seem to be obtained in young women who have the shortest history and the more severe form of the disease.

Bilateral Aneurysms of the Internal Carotid Artery: Successful Surgical Approach in One Stage. R. D. Weyand, E. F. Schmerl and J. L. Rhee. California Med. 91:79-83 (Aug.) 1959 [San Francisco].

When intracranial aneurysm is suspected, carotid arteriography should be done not only on the suspected side but always on both sides. Without surgical intervention, the prognosis of bilateral aneurysms is notoriously poor. With the aid of hypothermic anesthesia, it is now possible to operate on both sides in a single procedure. The authors report on a 43-year-old woman in whom carotid angiograms showed 2 aneurysms extending medially from the supraclinoid portion of each carotid artery. Hypothermic anesthesia was started with the aid of a cooling mattress. When the body temperature, measured with an esophageal thermometer, was below 34 C (93.2 F), operation was begun.

The aneurysms were approached by elevating the right frontal lobe, while cerebrospinal fluid was withdrawn from the lumbar region. Both aneurysms were identified. They were touching each other. During the attempt to dissect the right aneurysm from its bed, the left aneurysm ruptured at its fundus. Carotid arteries were occluded in the cervical region, and bleeding was greatly reduced. While the left aneurysm was being dissected free, both carotid arteries were occluded simultaneously for 10 minutes. After this, the arteries were released for 2 minutes and then occluded again for 8 minutes. During this time the left aneurysm was occluded to an area flush with the left carotid artery by means of 4 broad silver clips. After this, the right aneurysm was dissected free, and a 2-0 silk ligature tied about its base. The aneurysm decreased in size immediately. The esophageal body temperature reached 31 C (87.8 F). The patient remained on the cooling mattress, which was kept at a temperature of 34 C, for 2 days.

The patient was ambulatory within 3 weeks of operation. She resumed her normal activities and remained remarkably well, with the exception of minor complaints of headache and tenderness at the site of the cervical incision. The use of hypothermic anesthesia in this case was perhaps of decisive import. It appears to have helped in the control of cerebral edema at the time of operation, so that simultaneous bilateral approach could seriously be considered. Since it reduced the oxygen demand in the brain, it allowed a longer safe period of carotid occlusion. It is believed that continuation of use of the cooling mattress into the postoperative period helped control the usual postoperative hyperthermia and reduce postoperative cerebral edema.

Cancer of the Thyroid: A Twenty-Year Follow-up. J. W. Nadal. Am. J. Surg. 98:190-195 (Aug.) 1959 [New York].

The author selected from the records of 3,602 patients, who had thyroid operations at the Portland (Ore.) Clinic between 1916 and 1938, 31 with verified cancer of the thyroid. Thirteen had papillary carcinoma, 8 had follicular carcinoma, 6 had undifferentiated carcinoma, 1 had Hürthle-cell carcinoma, and in 3 the tumor was not classified histologically. A complete follow-up has been obtained in all 31 patients. Of these, 27 had bilateral subtotal thyroidectomy, 2 had total thyroidectomy, 1 had tracheostomy, and 1 had removal of tissue for biopsy. Nineteen of the 31 patients received postoperative irradiation therapy, 17 having radium and 2 X-rays. As would be expected, the 13 patients treated for papillary carcinoma had the best results. Of these, 11 appeared to have been cured; 5 of them died of unrelated causes many years later, and 6 are alive today, 21 to 32 years after their operations. In contrast, all 6 patients with undifferentiated type of cancer died within one year. In the entire group of 31 patients, 18 appeared to have been cured. There was no evidence that the postoperative irradiation therapy employed altered the end-results.

The Hemodynamic Results of Surgery for Aortic Stenosis. W. L. Kraus, R. C. Schlant, C. B. Moore and others. Am. Heart J. 58:174-189 (Aug.) 1959 [St. Louis].

The authors report on 12 men, between the ages of 25 and 59 years, and 7 women, between the ages of 37 and 55 years, who were operated on for aortic stenosis at the Peter Bent Brigham Hospital in Boston, and who were studied by left heart catheterization before and after transaortic valvuloplasty. The cardiac index was normal in patients with pure aortic stenosis but tended to be reduced in the presence of associated aortic regurgitation, mitral or coronary disease. Severe aortic stenosis, as it progresses, may become associated with a reduced cardiac output and, therefore, a small systolic mean pressure difference across the aortic valve. There was a small but significant postoperative increase in calculated aortic valve area in 11 patients, associated with a marked lowering of left ventricular systolic pressure, transvalvular pressure difference, and left ventricular work, while cardiac output remained unchanged. A residual pressure difference across the aortic valve persisted in all but one patient, in whom severe regurgitation developed.

Eight patients showed no change in valve area. The left ventricular systolic pressure and the transvalvular pressure difference in these were also decreased postoperatively, but this was found to be the result of reduced cardiac output. Associated mitral stenosis, mitral regurgitation, or coronary disease did not preclude successful surgery for aortic stenosis. Six of the 8 operative failures occurred among 7 patients with clinically "insignificant" preoperative aortic regurgitation as the only complicating lesion. Operation in this group either did not relieve the stenosis or increased the regurgitation in proportion to the relief of stenosis, so that measurable benefit was not observed. The term "insignificant" as applied to aortic regurgitation implies that preoperatively only an aortic diastolic murmur of minor degree was present, without any of the peripheral stigmata of aortic insufficiency. Were this the sole lesion, it would indeed be insignificant. The added transvalvular flow imposed by regurgitation, however, aggravates the manifestations of stenosis in proportion to the amount regurgitated. If aortic stenosis is severe, any regurgitation thus becomes significant. Hence, the term "insignificant" regurgitation, as applied to the 7 patients, has been enclosed in quotation marks. The lack of hemodynamic improvement in 6 patients may well indicate that the associated aortic regurgitation was by no means insignificant. The authors believe at this time that in the presence of severe aortic stenosis the assessment of otherwise insignificant regurgitation remains to be clarified.

In the presymptomatic phase of aortic stenosis, surgical treatment does not appear to be indicated. Until anginal pain, syncope, or failure appears, the medical prognosis is excellent and much better than the surgical. With the advent of any of this triad of complications, the medical prognosis is poor, while the surgical risk is between 8 and 10%. If aortic stenosis is severe and the patient symptomatic, surgical treatment should be carried out even in the presence of mitral stenosis, mitral regurgitation, or coronary disease. Associated aortic regurgitation, even of clinically minor degree, frequently appears to be unrelieved and possibly even enhanced by the present surgical approach to aortic stenosis. Operation on such patients should probably be withheld until evidence accumulates that regurgitation can be dealt with successfully.

Patent Ductus Arteriosus in Adult Life. G. H. Fairley and J. F. Goodwin. Brit. J. Dis. Chest 53:263-277 (July) 1959 [London].

The authors report on 12 men and 31 women, between the ages of 21 and 66 years, with patent ductus arteriosus, who were admitted to Hammersmith and St. Bartholomew's Hospitals in London during the last 10 years. The chest roentgenograms of the 43 patients showed enlargement of the main pulmonary artery, but except for this only common feature the patients fell into 2 distinct groups differing in most other respects. The first group consisted of 40 patients (93%) with a left-to-right shunt. Twenty-four (60%) of these had dyspnea on exertion, 10 (25%) had left submammary pain, and 3 had classical anginal pain. Twelve patients, who were symptomless, were referred because of a murmur which had been discovered during the course of a routine medical examination. Patients with a patent ductus arteriosus may remain symptomless until middle life, but may then deteriorate rapidly. Angina of effort, not previously described, may occur and is thought to be due to increased left ventricular work rather than to coronary artery disease, although the latter may explain the marked preponderance of women over men in later life. The classical continuous murmur of Gibson was heard in 39 of the 40 patients; the one exception was a patient with a recanalized duct, which was closed while infected; 9 patients had a mitral diastolic murmur representing a large shunt. Seventeen of the 40 patients underwent cardiac catheterization, and the total pulmonary resistance was normal (below 4 units) in 8 patients, and was elevated to 6 units in one patient only. The pulmonary resistance may remain normal for many years despite a greatly increased pulmonary blood flow, and there was no tendency for the pulmonary resistance to rise with increasing age.

Thirty-six of the 40 patients in the first group were treated surgically. Thirteen became symptom-free, 10 were improved, and 1 was unchanged after the closure of the duct. Twelve patients were symptomless before the operation, and of these 11 remained so, while dyspnea on exertion occurred in one after closure of the duct. There were no deaths as a result of the operation. In all the patients the diastolic blood pressure rose, and in most the size of the heart was reduced. The continuous murmur and the mitral diastolic murmur were abolished. Thus, against the almost certain development of disability in later life, together with a reduced life span, there must be considered the advantages of safe and complete curative operation with a low mortality. The authors, therefore, recommend that all patients with a patent ductus arteriosus and an appreciable left-to-right shunt should receive surgical treatment, regardless of age and lack of symptoms. The second group consisted of 3 patients (7%) with patent ductus arteriosus associated with a right-to-left shunt due to pulmonary hypertension (Eisenmenger reaction). These patients were between the ages of 30 and 48 years, and in them operation was not advised because of the high mortality.

Primary Endocardial Fibroelastosis. J. W. Lamb and C. P. Bernet. Am. Surgeon 25:549-551 (Aug.) 1959 [Baltimore].

The authors report on 3 female infants, between the ages of 16 and 24 months, and 2 male infants, aged 14 and 20 months, with primary endocardial fibroelastosis, who were studied at a community hospital in Greenwood, Miss., in the course of 2 years. This city has a population of 20,000. Primary endocardial fibroelastosis is a diffuse thickening of the mural endocardium, especially of the left ventricle, consisting predominantly of fibrous and elastic tissue without associated cardiac malformations or other demonstrable cause. Surgical treatment was refused by the parents of the youngest of the 3 female infants; this patient is alive 6 months after the diagnosis was made but is doing poorly. The second girl never recovered from cardiac failure after entering the hospital, and the third died of a cerebral embolus while she was being prepared for surgical intervention.

The 2 male infants underwent surgical therapy based on the altered physiology of ischemia of the myocardium. The pericardial sac was opened widely anterior to the phrenic nerve and pericardiophrenic vessels. Pericardial fluid, frequently abundant, was completely aspirated, and about 5 Gm. of sterile U.S.P. talc was placed evenly over the surface of the left ventricle primarily and, to a less degree, over the anterior surface of the right ventricle. The pericardium was then closed with interrupted silk sutures; a thoracotomy tube was placed into the inferior portion of the left pleural space; and the chest wall was closed in layers. The procedure was simple, being performed rapidly and being adaptable to poor surgical risk patients. Nevertheless, one of the boys died on the first postoperative day. The other improved after the operation, with gain in weight, normal development, and less symptoms of cardiac failure; however, the size of the heart did not decrease postoperatively, and this second boy died 19 months after the poudrage procedure. It is felt that surgical management should be considered in all such patients because of the uniformly poor prognosis with medical management.

Intracardiac Pressure in Constrictive Pericarditis. M. Foscarini, F. Boni, R. De Marchi and others. Clinica 19:151-160 (no. 2) 1959 (In Italian) [Bologna, Italy].

The right heart pressure was recorded by cardiac catheterization in 7 patients with constrictive pericarditis—in 6 preoperatively and postoperatively and in 1 only postoperatively. The symptoms were severe in all the patients, and consisted of edema in 6 and of marked ascites in 3. One patient died a few days after the operation of liver insufficiency; 3 were followed for a period of up to 5 months. Intracardiac pressure tracings revealed higher than normal pressure. There was a marked hypertension in the large tributary veins to the right heart. The intracavitary pressure pattern of the right ventricle in 5 patients revealed a normal systolic rise, followed by an early diastolic dip and a rapid rise to form a plateau. There was a considerable divergence between the early and the final stage of the diastole of the ventricular pressure and a decrease in the pressure gradient of the right atrium to the pulmonary artery.

The levels of mean atrial, final ventricular diastolic, pulmonary diastolic, and pulmonary capillary pressures were close to one another. A high capillary pressure reflected the pulmonary venous stasis. These recordings demonstrated that constrictive pericarditis involved both ventricles. The atrial pressure tracings showed M-or-W-shaped contours and a prominent *a* wave. The preceding patterns were characteristic but not specific of constrictive pericarditis. The results of some operations were very prompt and of others tardy, the latter being probably related to the myocardial condition.

Functional Aortic Stenosis: A Malformation Characterized by Resistance to Left Ventricular Outflow without Anatomic Obstruction. A. G. Morrow and E. Braunwald. Circulation 20:181-189 (Aug.) 1959 [New York].

When the clinical aspects of aortic stenosis are present and a pressure gradient is demonstrated between the left ventricle and the aorta, a discrete obstruction, generally amenable to surgical correction, has been assumed. The fallacy of this widely held concept is emphasized by the surgical and hemodynamic findings in the 3 patients presented in this report. These patients had functional obstruction to the left ventricular outflow. In 2 of them, although a significant pressure gradient was shown to exist between the left ventricle and the aorta and the obstruction was localized within the left ventricle, at the time of open-heart operation, no localized stenotic area was found. The authors feel that the obstruction must be attributed to systolic narrowing of the ventricular outflow tract resulting from massive muscular hypertrophy, the cause of which is obscure. Such narrowing was subsequently demonstrated in one patient by selective angiocardiography with left ventricular injection. In the third patient, functional aortic stenosis was present after surgical relief of a discrete subvalvular stenosis and regressed in the postoperative period.

The recognition of functional aortic stenosis is of importance, since this lesion is not amenable to surgical correction, and an unnecessary exploration of the ventricle and valve in such a patient is hazardous. The diagnosis may be suggested by certain features present in both the patients described. The systolic thrill and murmur were most prominent at the apex and lower left sternal border and less apparent in the aortic area. The thrill was not transmitted to the carotid vessels. Phonocardiography in the first patient revealed a loud holosystolic murmur at the apex, with a softer ejection murmur at the base of the heart. The second patient had a typical ejection murmur only. Poststenotic dilatation of the aorta was not demonstrable. This latter finding is in contrast to that in patients proved to have the more usual form of congenital subvalvular aortic stenosis. In both patients at left heart catheterization, the obstruction was demonstrated to lie beneath the aortic valve. Thus, it would seem that the diagnosis of functional aortic stenosis can be excluded by the demonstration of a pressure difference across the valve and must be suspected when the site of stenosis is shown to be below it. For this reason complete left heart and aortic catheterization would seem preferable to simple ventricular puncture in the study of patients with aortic stenosis. It is probable that selective left ventricular angiography would prove the most definitive diagnostic technique in distinguishing this lesion from the other forms of aortic stenosis and would also reveal any accompanying mitral insufficiency. The persistence of a large pressure gradient after complete relief of a localized subvalvular obstruction in the third patient can only be attributed to functional aortic stenosis.

Pericardiectomy for Massive Recurrent Pericardial Effusion. R. J. Jaffe and H. Kallman. Ann. Int. Med. 51:363-371 (Aug.) 1959 [Lancaster, Pa.].

A history is presented of a 61-year-old woman, who had been well until 11 months before admission to Kings County Hospital Center, Brooklyn, N. Y. At that time she experienced substernal, epigastric, and right upper quadrant pain. Three weeks after the onset of symptoms she was hospitalized at another hospital, where examination revealed a pericardial effusion. Three pericardicenteses were performed, and a total of 1,400 cc. of hemorrhagic fluid was removed. "Atypical cells" were found, said to be "indicative of adenocarcinoma." Induced pneumopericardium showed increased thickness of the parietal pericardium. Chest films revealed a "small infiltrate in the left midlung field," but the etiology could not be definitely established. The patient was discharged as improved, but 6 months later she was readmitted to the same hospital with mild cyanosis, anasarca, cardiomegaly, distant heart sounds, a systolic murmur at the aortic area, and hepatomegaly. Treatment consisted of 3 pericardial taps; the first one of these yielded 1,800 cc. of hemorrhagic fluid, examination of which did not reveal atypical cells, bacteria, or fungi. The patient was discharged as improved in February, and entered Kings County Hospital Center in May, with massive anasarca, despite treatment with digitalis, diuretics, and low-sodium diet. Thoracentesis yielded 500 cc. of straw-colored fluid, and during the next 3 days 3 pericardicenteses were performed, and a total of 3,880 cc. of chocolate-colored fluid was removed. This again was followed by improvement, and additional studies were performed, all of which, including scalene node biopsy, were negative.

When symptoms of heart failure returned despite the use of digitalis, low-sodium diet, and diuretics, thoracotomy and pericardiectomy were carried out. The epicardium was covered with a thin layer of greenish yellow exudate resembling "sugar icing." No evidence of tumor could be found. Microscopic study of the pericardial tissue confirmed the suspicion of idiopathic pericarditis. The patient was asymptomatic one year after the operation. The similarity between chronic idiopathic pericarditis and constrictive pericarditis as to both the clinical picture and the response to pericardiectomy deserves emphasis. The case presented illustrates the failure of prolonged medical management and the good results that may follow surgical correction even after prolonged cardiac tamponade.

Congenital Coronary Arteriovenous Fistula Associated with Large Patent Ductus. L. H. Bosher Jr., S. Vasli, C. M. McCue and L. F. Belter. Circulation 20:254-261 (Aug.) 1959 [New York].

The female infant whose history is presented showed symptoms of cardiac failure at the age of 4 months. At 16 months generalized edema and hepatomegaly developed, and the child was digitalized. On March 19, 1956, at 18 months, she was admitted to hospital for study. The tentative diagnoses were interatrial septal defect and patent ductus arteriosus. Interventricular septal defect and pulmonary insufficiency were also considered. A retrograde brachial aortogram was advised, but the family refused. The child was readmitted to the hospital on Dec. 28, 1956. There was suggestive enlargement of the left ventricle. Increased pulsations were seen in the pulmonary vascular bed on fluoroscopy. A retrograde aortogram was performed through the right brachial artery. Now a tentative diagnosis of large patent ductus arteriosus with pulmonary insufficiency and tricuspid insufficiency was made. The possibility of a ruptured sinus of Valsalva into the right ventricle was also considered, but the proper interpretation of the aortogram was not made. The patient was admitted a third time for surgery on May 11, 1957. At the time of admission there was evidence of bronchopneumonia.

Operation was carried out through a bilateral transsternotomy incision 17 days later, after clearing of the pneumonitis. The pump oxygenator was prepared for possible use. A large patent ductus was found. After division of the ductus there remained a thrill over the right atrium. Further examination revealed a vessel, roughly 0.5 cm. in diameter, branching from a dilated left coronary artery and passing through the transverse sinus behind the aorta and pulmonary artery to empty into the right atrium behind the origin of the superior vena cava. The anomalous coronary vessel was ligated with several sutures near its entry into the atrium. The postoperative course was uneventful for 24 hours, but the child died apparently of a cardiac arrhythmia 30 hours after the operation.

The authors point out that several reviews have been published recently describing the anatomic and clinical findings in patients with congenital coronary arteriovenous fistulas or with communications between the coronary arteries and the cardiac chambers. The recognition of this clinical entity presents real difficulty, since it may easily be confused with other lesions causing a continuous or to-and-fro murmur, such as patent ductus arteriosus, aortopulmonary septal defect, ruptured aneurysm of an aortic sinus, interventricular septal defect with aortic insufficiency, and arteriovenous communications within the chest wall or lungs. The authors collected 38 cases of congenital coronary arteriovenous fistula from the literature. They analyzed these 38 cases together with their own (39th). The right coronary system was involved in 19, and the left coronary system in 16 cases. In 2 cases both right and left coronary artery systems participated, and in the remaining cases information regarding the exact anatomic arrangement was not available. Associated congenital defects, which were encountered in 6 cases, included pulmonary atresia, pulmonary atresia with interventricular septal defect, single ventricle, and patent ductus in 2. The case presented is the second one in which the left coronary artery system communicated directly with the right atrium, and also the second case associated with a patent ductus.

Cardiac Aneurysm with Ventricular Tachycardia and Subsequent Excision of Aneurysm: Case Report. O. A. Couch Jr. Circulation 20:251-253 (Aug.) 1959 [New York].

The woman, whose history is presented, was 54 years old when first seen in September, 1953. Her ventricular tachycardia was controlled only with rather exactly regulated doses of quinidine sulfate. Administration of this drug was continued until the time of operation. After excision of a ventricular aneurysm, quinidine was withdrawn without further recurrence of the tachycardia. This sequence suggests that an irritable focus causing the tachycardia had been removed with removal of the aneurysm. Despite the cardiac arrest at the time of operation, the patient's postoperative recovery has been excellent. She has gained strength progressively and has reached a considerably higher level of activity than was possible prior to operation.

Extramucosal Cardiomyotomy According to Heller's Technique in the Treatment of the So-Called Idiopathic Megaesophagus. F. Cecconi. Arch. ital. chir. 85:135-152 (no. 2) 1959 (In Italian) [Bologna, Italy].

The author reports on 38 patients (20 men and 18 women) with idiopathic megaesophagus observed at the surgery clinic of the University of Rome from 1950 to July, 1957. Extramucosal cardiomyotomy through the abdomen (Heller's operation) was performed on 31 patients. Dysphagia, frequently combined with regurgitation, was the initial symptom in most instances. A weight loss of from 3 to 20 kg. (7 to 44 lb.) was noticed in all the patients. The Delbet-Zaaijer variation of Heller's operation was followed. A longitudinal incision was made on the anterior cardioesophageal wall. Approach was made through a median xiphoumbilical incision; removal of the xiphoid and partial mobilization of the costal cartilage was resorted to in a few cases only. Resection of the left triangular ligament of the liver, but not of the coronary ligament, was indispensable in all instances. A good exposure of the cardia and of the terminal segment of the esophagus was of fundamental importance; on it depended the possibility of performing an adequately long cardiomyotomy; this should extend from 2 or 3 cm. below the cardioesophageal junction to at least 7 cm. above the beginning of the dilatation of the esophagus.

Laceration of the gastric or esophagus mucosa occurred once, but it was checked immediately and resulted in no complications in the postoperative course. All 31 patients survived the operation. Immediate results, especially from the functional point of view, were good in all instances; dysphagia disappeared, normal alimentation could be resumed, and body weight increased. On late observations made from 7 months to 6 years after the operation, results were still good in 21 patients, but they had deteriorated partially in 8, and had become poor in 2; the latter patients presented marked, and at times even painful, dysphagia, frequent and marked regurgitation, peptic esophagitis, and progressive loss of weight. The best results were obtained in persons under 40 years of age. These were mainly women, since most of the male patients were between 40 and 60 years of age.

The Radiological and Bacteriological Assessment of Tuberculous Lung Lesions Remaining After Chemotherapy. A. W. T. Eade, G. K. Harrison, S. E. Large and others. Thorax 14:104-112 (June) 1959 [London].

Partial lung resection was performed on 59 Gurkha soldiers with pulmonary tuberculosis at an army chest center in England after a regimen of chemotherapy for periods of between 10 and 25 months. Initially the patients received streptomycin, 1 Gm. daily, and isoniazid, 100 mg. twice daily, for either 30 or 60 days. Then both drugs were given in the same dosage every other day until operation. There was roentgenologic evidence of cavitation on admission in 39 patients (66%). In these patients the presence of 46 cavities was confirmed roentgenologically. Forty-one cavities which had been present at the beginning of treatment in 34 patients closed before operation, but 5 large cavities were still present at the time of operation in the remaining 5 patients. The lesions from 3 of the latter were culture-positive, the organisms in 2 being resistant to streptomycin and isoniazid.

Of 34 instances in which the solid residuum of previously cavitated disease was resected, tubercle bacilli were cultured from the specimen in only one patient, and then not from the cavity itself. This patient had received chemotherapy for only 4 months after the cavity had closed, whereas 30 of the remaining 32 patients had received such treatment for from 6 to more than 18 months. Of 20 patients with noncavitary disease, tubercle bacilli were cultured from the resected specimen in only 2 who had received chemotherapy for 14 and 16 months respectively. Both of the latter patients had been consistently sputum-negative, had negative preoperative laryngeal swabs, and had shown only slight roentgenologic change during treatment. This study suggests that the persistence of viable tubercle bacilli in the lesions is reduced with the increased duration of chemotherapy, unless bacterial resistance to the drugs used in treatment has developed.

A Planned Study of Minimal Tuberculosis. R. Douglass, E. M. Medlar, N. S. Lincoln and others. J. Thoracic Surg. 38:191-208 (Aug.) 1959 [St. Louis].

An analysis of 104 patients with minimal tuberculosis regarded as clinically active, who were treated by bed rest, chemotherapy, and resection of residual lesions, is presented, together with data from pathological studies of each surgical specimen. There were 43 men and 61 women, between the ages of 10 and 59 years. Chemotherapy, such as streptomycin, para-aminosalicylic acid, or isoniazid in some combination, was given for from 4 to 8 months preoperatively. After the operation chemotherapy was at first given to cover the recovery period, but when excised specimens revealed areas of new disease which had occurred during the drug therapy, the drugs were arbitrarily given for about 4 months postoperatively.

Major complications of surgery occurred in 11 patients, but all responded well to therapy. Minor complications were seen in 15 patients, and all recovered. There was no operative death. Of the 104 cases, a total of 119 lungs were explored, and the lesions excised; on 15 patients a bilateral excision was performed, and on 89 a unilateral one. Not infrequently more disease was found at operation than was suspected from chest roentgenograms, and, on occasion, lesions were found in areas not suspected preoperatively. Because of extensive developmental bronchiectasis, a right lower lobe with tuberculosis was removed in one case. In the remaining 118 lungs only segments or subsegments were excised. These findings indicate that, as long as the disease remains minimal in extent roentgenologically, it is essentially a localized process.

In the study of pathology, one case showed parenchymal scarring only. All other specimens showed multiple necrotic lesions and scarring but with considerable variations both in size and number of necrotic foci and amount of scar. There were considerable differences in the ages of the various types of lesions, not only from case to case but within single specimens. The specimens revealed necrotic lesions in 103 patients, this being the dominant feature in 83. Bronchial communication was demonstrated in 49 patients, and was believed to exist in all necrotic lesions. Cavity formation was demonstrated in 48 patients—open in 14, "filled in" in 30, and largely scar in 4. Pneumonic foci, interpreted as recent bronchogenic spreads, were noted in 10 patients despite chemotherapy. There was no correlation noted between the duration of chemotherapy and the anatomic pathological features which varied widely; nor was there a demonstrable causal relationship between chemotherapy and the observed features of the necrotic (caseous) lesions, which had not been eradicated.

Ninety-eight patients were followed up for from 1 to 6 years. Two patients died—one in the 2nd postoperative year of bronchogenic carcinoma, and the other in the 5th year because of gangrene of the lower extremities. In one patient a clinical relapse occurred in the 5th postoperative year.

Scalene Lymph Node Biopsy, Cytologic Studies, and Other Diagnostic Methods in Intrathoracic Disease. A. Gaurie and G. H. Friedell. J. Thoracic Surg. 38:235-243 (Aug.) 1959 [St. Louis].

The authors compared the results of scalene node biopsy and those of exfoliative bronchial cytology performed in 100 consecutive patients between 1951 and 1958. They also reviewed the relative effectiveness of the various techniques used in the diagnosis of intrathoracic disease, namely, roentgenologic studies, bronchoscopy, scalene node biopsy, and exfoliative cytology. Cases were included in this series only if the node biopsy was done to assist in the diagnosis of intrathoracic disease. In most of the cases, the nodes removed were not palpable before operation. All cases in which tissue was submitted to the laboratory, regardless of the number of nodes identified, were included. A diagnosis of tumor was made by the bronchoscopist in 43 of 62 patients with intrathoracic neoplasms. Scalene node biopsy specimens were positive for tumor in 37 of the 62 patients with intrathoracic tumors. Cytological preparations were usually made in cases which were diagnostic problems, and were not made in several cases with clinically obvious neoplastic disease. Thus, 48 Papanicolaou smears were prepared, of which 8 were reported as positive, and in all 8 cases intrathoracic tumors were present. The slides from 2 cases were considered inadequate for diagnosis. The remaining 38 smears were reported as negative, although in 27 of these 38 cases a final histological diagnosis of intrathoracic malignancy was made. In 10 of these 27 cases, a positive diagnosis was made on the scalene node biopsy specimens.

The relatively low diagnostic accuracy of the cytological studies is attributed primarily to deficiencies in the techniques used in preparing the smears. It is felt that more satisfactory cytological preparations can be made after centrifugation of the specimen; it would then be essential that a definite routine be established and that the responsibility for performing the necessary procedures be specifically assigned to one person in either the surgical or the laboratory service. Without such a designated routine supervised by one individual, variation in procedures seems quite likely to occur without the knowledge of either the collector of the specimen or the interpreter of the final preparation. On review of smears originally called negative, about 30% were found to be insufficient for definitive diagnosis. If these inadequate smears are not considered, the diagnostic accuracy of the cytological material becomes 34% in cases of intrathoracic tumor. Each of these 3 diagnostic methods, bronchoscopy, scalene node biopsy, and cytological study, is felt to have a definite place in the diagnostic armamentarium, and each would appear to be most useful as a complemental technique rather than as a replacement for the other two.

Scalene Node Dissections. J. W. Castleberry, D. J. Davis and R. B. Trumbo. Am. Surgeon 25:552-556 (Aug.) 1959 [Baltimore].

Scalene node dissection has become a useful and fairly well standardized method in the diagnosis and management of thoracic diseases. Surgeons undertaking these procedures are reminded, however, of the many shortcomings observed, and of the many responsibilities which must be discharged to give maximal value to the dissections. This is a hazardous, time consuming, and only slightly revealing procedure. All other diagnostic methods short of thoracotomy should be used before scalene node dissection. Complications may include injury of major or minor nerves, hemorrhage, lymphatic fistula, pneumothorax, air embolism, and infection. The operative time averages 1¼ hours. Delay in treatment results unless the dissection is combined with bronchoscopy or other diagnostic methods. Complete examination of the specimen is of great importance. These nodes are seldom positive with a known primary diagnosis of bronchogenic squamous-cell carcinoma. If no nodes are palpable, only 8 to 10% of all dissections will reveal positive nodes. A distinction should be made between biopsy and dissection. Biopsy should refer to the removal of a small portion of tissue, such as a wedge from a supraclavicular mass, or a single suspected node. Dissection should indicate a clean sweep of regional nodes.

Adrenalectomy in the Treatment of Advanced Breast Cancer. W. H. Parsons and S. G. Blackshear. Am. Surgeon 25:604-606 (Aug.) 1959 [Baltimore].

The authors performed bilateral adrenalectomy on 25 women, between the ages of 24 and 71 years, with far-advanced, severely painful cancer of the breast, who had failed to obtain any relief from all forms of therapy and who faced an undeniably hopeless prognosis. Unequivocally beneficial results, sometimes dramatic, were obtained in 10 of 20 patients. In 5 patients it has been too soon after the operation for an evaluation to be made. There was only one postoperative death. The mean survival time for the 10 patients who did not respond to adrenalectomy was 4.9 months. Of the 10 patients who were benefited, 4 are alive 19, 10, 8, and 3 months after the adrenalectomy. The mean survival time was 17.8 months for the 6 patients who did respond but have died. The results obtained in this group of patients and in 934 patients whose cases were collected from the literature justify the conclusion that bilateral adrenalectomy has definite, often dramatic beneficial effects in certain women with advanced metastatic carcinoma of the breast. The total number of patients who have had adrenalectomy is now large enough, the postoperative period sufficiently long, and the survival rate favorable enough to suggest its performance whenever the prognosis would otherwise be hopeless.

By no means, however, are all patients benefited by this procedure. The crucial matter, therefore, is to determine which patients will respond favorably to removal of the adrenal glands. The authors do not agree that one can determine from the cellular pattern of the lesions which patients will be helped by adrenalectomy. Clinical evidence indicates that the woman most apt to be benefited by adrenalectomy is one in the premenopausal age who has had a temporary favorable response to oophorectomy. Since patients with cancer of the breast who have undergone oophorectomy often continue to excrete estrogen in the urine, and since the adrenal glands are a source of this hormone, the combination of adrenalectomy with oophorectomy seems reasonable. All sources of sex steroids, on which certain cancers from mammary epithelium retain their dependency after oophorectomy, would thus be eliminated.

Esophageal Replacement and Bypass with the Ascending and Right Half of the Transverse Colon for the Treatment of Congenital Atresia of the Esophagus. J. S. Battersby and T. C. Moore. Surg. Gynec. & Obst. 109:207-215 (Aug.) 1959 [Chicago].

The authors review the literature pertaining to the use of the right half of the colon for esophageal replacement in the management of congenital atresia of the esophagus. A need for esophageal replacement exists in the infrequent case of esophageal atresia with tracheoesophageal fistula in which there is insufficient length of the 2 esophageal segments for primary end-to-end anastomosis and in virtually all cases of the rather small group of atresias without fistula in which the distal esophageal segment generally is partially or completely absent. The initial management of these 2 types of cases at birth is discussed. The authors report on the use of the right half of the colon for esophageal replacement in 5 children with congenital atresia of the esophagus, who were observed at the Indiana University Medical Center, Indianapolis. Four of the patients had esophageal atresia, no fistula, and absence of the distal esophageal segment, and one had atresia with tracheoesophageal fistula. The first child was successfully operated on in January, 1953. This patient is alive and doing well almost 6 years after operation.

The cecum was utilized for proximal esophageal anastomosis in 3 cases and the terminal part of the ileum in 2. All distal colonic transplant anastomoses were carried out into the anterior wall of the stomach. The substernal route with esophageal anastomosis in the neck was used in 3 cases, and intrathoracic colon transplantation with intrathoracic esophageal anastomosis was employed in 2. Three patients recovered, and 2 died. The 3 surviving patients were all in excess of 7 months in age and 16 lb. (7,257 Gm.) in weight at the time of operation. The substernal route with esophageal anastomosis in the neck was utilized in all 3. The surviving patients have been observed for 6, 2, and 1¾ years after esophageal replacement. The transplanted right half of colon has functioned satisfactorily as an esophageal substitute in all, and they have grown and developed in a normal manner. There has been no evidence of peptic ulceration in the colon transplant.

Both infants who died were managed by intrathoracic right half of the colon esophageal replacement with the esophageal anastomosis in the chest. One patient, a premature infant weighing 4½ lb. (2,040 Gm.), was operated on at 8 days of age and died 18 days after operation, with progressive loss of weight and suspected terminal intrathoracic anastomosis breakdown. The other patient was a malnourished 6-month-old infant who weighed only 9½ lb. (4,308 Gm.); this patient died 8 days after a breakdown of the intrathoracic anastomosis, which occurred 11 days after operation. Leakage with the formation of a fistula at the proximal esophageal anastomosis was the most frequently encountered postoperative complication. In those cases of congenital atresia of the esophagus in which esophageal replacement is required, the use of the right half of the colon through a substernal tunnel with proximal esophageal anastomosis in the neck is recommended.

Treatment of Wilms's Tumor. H. Bay-Nielsen. Ugesk. laeger 121:1190-1193 (July 30) 1959 (In Danish) [Copenhagen].

Wilms's tumor develops only in the kidney and metastasizes by both lymphogenic and hematogenic means. The initial symptoms are often vague. The most important later symptoms are hematuria, rapidly increasing abdominal circumference, and abdominal pain. The tumor grows rapidly through the renal capsule and expansively in the peritoneal tissue. Treatment in the last 25 years has been nephrectomy combined with roentgenotherapy. The Danish material has included 17 histologically verified cases. The average age of the patients at operation has been 2 years and 3 months. Palpation of the tumor was limited as far as possible. Preoperative treatment with fluids and transfusions was given. Nephrectomy was performed within a period of a few hours to 20 days after admission. The method was transperitoneal in 12 patients and thoracoabdominal in 4; in one patient a lumbar incision was made. The thoracoabdominal technique seems to present important advantages. Postoperative roentgen-ray treatment, given in 13 cases, was begun on the day of operation in 1 instance, during the first 3 days in 4, and later in the other cases. One patient died during the operation; 13 patients died from 2 months to 3⅓ years postoperatively. Three patients have survived for 10, 4½, and 2½ years respectively. Many patients are admitted late, in poor general condition, and with prominent tumor. If there are symptoms of Wilms's tumor, time is of the essence, and nephrectomy should be performed as soon as possible, with the assistance of pediatrician and anesthesiologist; roentgen-ray treatment should be given immediately after the operation.

Effectiveness of Treatment of Severe Ammonia Toxicity. W. Lawrence Jr., P. Vanamee, J. W. Poppell and H. T. Randall. Surg. Gynec. & Obst. 109:139-144 (Aug.) 1959 [Chicago].

The authors review their experience with the treatment of hepatic coma associated with ammonia toxicity. They evaluate the effectiveness of the treatment of patients having severe ammonia toxicity with the use of monosodium glutamate. The patients included were those in whom significant clinical signs and symptoms of ammonia toxicity developed in association with definite elevation of blood ammonia. All those exhibiting mild neurological symptoms (or stage 1, as described by Najarian) were eliminated, as they did not require aggressive amino acid therapy. Also rejected were patients who had ammonia toxicity secondary to obvious exogenous sources of ammonia, as they can generally be treated by simple elimination of the drug or compound. After this selection, there remained for study 96 patients with 100 separate episodes of ammonia toxicity. These patients exhibited either stupor (precoma) or frank coma.

Treatment of this group included the following measures: correction of electrolyte abnormalities; glucose infusions; blood transfusion when necessary; and administration of monosodium glutamate intravenously (usually 80 Gm. over a 24-hour period). Potassium chloride (80 to 120 mEq.) was administered parenterally during the same period to counteract the metabolic alkalosis produced by such large dosage of monosodium glutamate. Criteria of success or failure of therapy in each patient were correlated with the stage of coma as well as the clinical category of ammonia toxicity. These categories were as follows: surgical portal systemic shunt (8 patients); portal cirrhosis with gastrointestinal hemorrhage (22); severe hepatitis (6); portal cirrhosis without gastrointestinal hemorrhage (spontaneous liver failure, 35); and neoplastic replacement of the liver (29).

The results of treatment of combined supportive therapy with the intravenous administration of monosodium glutamate were tabulated for the entire group of patients in terms of decrease in blood ammonia (79.7%), clinical improvement in mental status (63%), and immediate survival (46%). The etiology of the ammonia toxicity was correlated with these criteria of therapeutic effectiveness. The findings suggest that ammonia toxicity secondary to circulatory bypass of the liver was more easily managed than those clinical situations in which the elevation in blood ammonia was secondary to hepatic dysfunction. Treatment of the elevation in blood ammonia in patients with advanced hepatic failure and coma appeared to be helpful; however, the results were far from ideal.

Cystic-Cholecystic Syndrome Due to Mechanical Blocking. D. Vasconcelos, F. L. Castro and E. Chaves. Rev. Assoc. méd. brasil. 5:128-137 (April-June) 1959 (In Portuguese) [São Paulo, Brazil].

The authors report on 24 patients with the cystic-cholecystic syndrome, all of whom were treated surgically. This syndrome is characterized by the blocking of the bile flow from the gallbladder into the choledochus, with consequent vesicular stasis, hyperpressure, and distention. In most cases the biliary blocking is caused by congenital malformations in the infundibulocholecystic area. The group of patients studied in this article included 18 women and 6 men, between the ages of 23 and 74 years. The clinical picture of the cystic-cholecystic syndrome is not characteristic; it resembles the common picture in cholecystic disease. The most frequent signs and symptoms in this series were hepatic pain, nausea, and diarrhea, in various degrees and forms. Two patients also had jaundice, which was difficult to explain in the absence of a choledochal process.

The most suggestive results of the 62 duodenal intubations performed on the 24 patients were longer time for the bile flow, and alterations in the gallbladder emptying time (which may be shortened, prolonged, or intermittent). The important radiologic features were a well-contrasted picture of the gallbladder, giving the impression of tension, and vesicular stasis, especially if it were associated with an abnormal contracting movement of the gallbladder. This abnormal contracting mechanism is translated in the radiologic picture by alterations in the shape of the gallbladder image, with a sharpening of the bottom area while the infundibular area is dilated. The gallbladder may also suffer a lateral upward displacement, nearing the ribs. Duodenal intubation and cholecystography are the most valuable means of diagnosis in the cystic-cholecystic syndrome. The results of these 2 types of examination should be combined and compared because of the variety of features in the individual cases.

The Surgical Correction of Calcific Aortic Stenosis in Adults: I. Technique of Transaortic Valvuloplasty. D. E. Harken, H. Black, W. J. Taylor and others. Am. J. Cardiol. 4:135-146 (Aug.) 1959 [New York].

The natural history of aortic stenosis differs significantly from that of mitral or tricuspid stenosis. The physiological derangement in aortic stenosis depends on 2 factors. First, the arteriosclerotic marginal leaflet fusion may cause a loud murmur or murmurs long before there is any hemodynamic disturbance. Second, even after there is valve impedance, there may be a long symptom-free period before rapid deterioration and death. The congestive failure, which heralds the onset of the terminal phase, may be due to the discrepancy between the muscle mass of the left ventricle and its blood supply. The ominous significance of left ventricular failure, as manifested by dyspnea on exertion, is emphasized.

The authors found that the commonest pattern of adult calcific aortic stenosis is fusion of the anterior and posteromedial cusps with little or no adherence of the edges of the noncoronary cusp. This results in a bicuspid valve with only a rigid, narrow slit for an opening. Nevertheless, an area of mobility or "hinge zone" can almost always be identified near one of the commissures. This pattern was present in 30% of the cases. The tricuspid pattern was also found in approximately 30% of clinical and autopsy specimens. The punctate form produces the most advanced narrowing with an orifice that may be no larger than a match head. There are many intermediate gradations of these basic patterns, but the outstanding common denominator of adult aortic stenosis is massive calcification and absence of mobility. The mechanism of valve closure in calcific aortic stenosis is quite unlike that of the normal valve. The surgeon undertaking corrective surgery must understand both mechanisms and their combinations.

Of 23 patients with pure aortic stenosis operated on by the original transventricular route, 10 died from the operation, and 10 more succumbed subsequently. After Swann demonstrated in 1954 that the aortic valve could be approached from above through an operating tunnel sutured to the wall of the aorta, the authors have employed a modification of this technique in 100 cases. Tunnels made of cotton, nylon, and polyethylene-lined nylon were used, but it was not until Hugh Wilson suggested the use of an Ivalon sponge tunnel that a satisfactory hemostatic method was developed. The Ivalon tunnel is prepared by wrapping 3 or 4 layers of moistened, thin-sliced Ivalon on the barrel of a 30-cc. syringe. The bottom edge of this tunnel is built up to a greater thickness to hold the sutures. Tight wrapping with gauze compresses it. Sterilization is accomplished by boiling. The individual operating tunnel, 3 or 4 cm. in length, is cut from this tube and sewn to the lips of the aortic incision with interrupted sutures through the full thickness of the aorta. These are first placed at the 4 quadrants of the incision, and the natural elasticity of the tunnel holds the aortic edges open for easy suturing. The second layer consists of a row of continuous silk suture, which forms a water-tight seal between the external edge of the Ivalon tunnel and the adventitia of the aorta. Although some oozing through the tunnel may occur when the clamp is first released, the interstices quickly fill with clots, and no further bleeding occurs. The mobilization of the valve leaflets, the removal of the tunnel, hemostasis, and the postoperative management are described.

There were 12 late deaths and 16 operative deaths among the first 100 patients treated by the transaortic technique, but the operative mortality has been reduced to 5 in the last 60 consecutive patients. Eighty-six per cent of the surviving patients followed from 6 to 36 months are improved. The gratifying salvage from this fatal disease encourages further use of this method of surgical relief.

Postoperative Physiopathologic Results in Mitral Stenosis. E. Coelho, A. Bordalo e Sa, J. Maltez and others. Am. J. Cardiol. 4:163-179 (Aug.) 1959 [New York].

The authors are concerned with the physiopathological changes which occur in patients with mitral stenosis after mitral commissurotomy. From the case material of the cardiology center of the Medical Faculty of Lisbon, they selected 200 patients who could be followed for long periods after the commissurotomy. These patients were studied at intervals of several months, 1 year, 2 years, or 3 years after the operation. Pericarditis occurred after the operation in 90% of the cases, and the postpericardiotomy syndrome (the so-called postcommissurotomy syndrome) in 12.5%, with no correlation between this and the results of biopsy of the auricular appendage. The results of mitral commissurotomy were evaluated by preoperative and postoperative cardiac catheterization, phonocardiogram, electrocardiogram, vectorcardiogram, electrokymogram, ballistocardiogram, roentgenogram, pulmonary angiocardiogram, and pulmonary function tests. The physiopathological data did not always correspond to the clinical results. Sometimes the clinical improvement was greatly superior to the results furnished by these tests.

Excellent or good clinical results were obtained in 67 to 70% of the 200 patients. Twelve patients (6% died. Factors inducing physiopathological results in mitral commissurotomy are discussed. These include postoperative mitral insufficiency, valvular calcification, postoperative emboli, insufficiency of the myocardium, subvalvular stenosis, insufficient commissurotomy, and recurrent rheumatic reactivation which may cause restenosis.

The Accomplishments of Open Heart Surgery: The Status of 35 Patients 18 to 36 Months Following the Operation. C. P. Bailey, B. G. Musser and D. P. Morse. Am. J. Cardiol. 4:147-154 (Aug.) 1959 [New York].

The authors review their experiences with 35 patients who underwent successful open-heart surgery with the aid of a pump oxygenator, and who are now alive more than 18 months after surgery. Twenty-three of the patients had aortic stenosis, and 2 had aortic insufficiency. Of the 10 patients with congenital defects, 3 had congenital aortic stenosis, 4 had tetralogy of Fallot, and 3 had ventricular septal defects. The Friedland-Gemeinhardt oxygenator, a modification of the DeWall apparatus, was used in all the patients. Two Sigmamotor pumps were used to replace, respectively, the right and left ventricles. The bodily venous return was withdrawn from the venae cavae through separate catheters, and the oxygenated blood was returned to the arterial circuit by way of a subclavian catheter. An additional Sigmamotor pump was used in some of the patients for retrograde perfusion of the coronary sinus with oxygenated blood. The rate of extracorporeal flow was maintained at nearly the patient's normal cardiac output (adult average, over 3,000 cc. per minute). The last patient in the series, operated on Aug. 21, 1957, was perfused by a new principle involving the use of the patient's own lungs as an oxygenator. Elective cardiac arrest was not used in this series, but since then arrest was used for a period of one year and now has been abandoned.

Although subjectively the patients with aortic stenosis were completely relieved, or at least greatly improved, the catheterization data in those who have returned for study show that in these early open procedures for aortic stenosis the authors failed to bring about a return to normal pressure and flow relationships. Because of the severe degree of valvular calcification, fibrosis, and rigidity of the valve leaflets, a complete obliteration of the pressure gradient was not obtained. Recently a new technique has been developed for removing the calcium and much of the scar tissue from the concave side of each cusp. This "sculpturing" restores mobility and function to the valve to a near-normal extent. In one of the patients with congenital aortic stenosis, a significant amount of aortic insufficiency was produced. Both of the patients with pure aortic insufficiency, who have survived more than 18 months after plication and resection of the noncoronary bearing cusp of the aortic valve, remain improved. Aortic regurgitation has been greatly reduced, and the signs of congestive heart failure, angina pectoris, and the palpitation previously present in each case have disappeared.

The ages of the 4 patients with tetralogy of Fallot ranged from 2 to 22 years. Defects in the membranous portion of the interventricular septum were repaired with simple or mattress sutures. In one case this was supplemented by Ivalon pledgets to reinforce the mattress sutures. The protruding portion of the supraventricular wall was resected in the 3 cases in which obstruction was of the infundibular type. In the patient with purely valvular stenosis, the pulmonary artery was opened, and the commissures were incised along the line of congenital fusion. In the 2 patients in whom postoperative catheterization studies have been carried out, complete cure has been demonstrated. In each of 3 patients with ventricular defects, closure was accomplished by simple suture.

Excellent improvement persists in 34 of the 35 patients. The authors feel that the results of their experience with open-heart surgery clearly demonstrate that certain defects, which cannot be treated adequately by the techniques of closed-heart surgery, now may be relieved, or even "cured," with an open technique made possible by the use of the pump oxygenator. They anticipate that the results of more recent work with the open-heart procedure will be better than in these early cases.

The Dumping Syndrome: II. Further Investigations of Etiology in Patients and Experimental Animals. H. W. Scott Jr., M. G. Weidner Jr., H. J. Shull and A. G. Bond. Gastroenterology 37:194-199 (Aug.) 1959 [Baltimore].

A previous study of the dumping syndrome in 31 patients who had undergone gastrectomy revealed an excellent correlation between the clinical occurrence of the syndrome and the symptoms and blood volume alterations induced by a standard test meal of 150 cc. of 50% glucose. In the present investigation 5 patients who had no clinical dumping symptoms after a gastrectomy and who had failed to respond to the initial test meal were retested, 300 cc. of 50% glucose being used; each developed severe dumping symptoms and a sharp drop in blood volume. Ten normal persons were tested by injection of 200 to 300 cc. of 50% dextrose directly into the jejunum through a plastic intestinal tube; each developed typical dumping manifestations with concomitant acute decreases in blood volume. None of 5 normal controls who took 150 cc. of 50% glucose orally showed any change. In a second group of 5 normal subjects, one person who drank 300 cc. of 50% glucose had minor symptoms and a significant blood volume reduction. The changes in blood volume in dogs in response to the intrajejunal administration of 50% dextrose in varying amounts followed the same pattern as found in the 10 clinical subjects.

These data emphasize the validity of the "hyperosmolar-hypovolemia" concept of the mechanism of the dumping syndrome and demonstrate that an adequate hyperosmolar concentration in the upper jejunum will produce all the phenomena of dumping in both normal and gastrectomized persons. The observations revealed that small amounts of hyperosmolar material are well tolerated, whereas large amounts produce the florid syndrome. In addition to the quantity of hyperosmolar material ingested orally, the extent of gastric resection and the type of gastrointestinal anastomosis appear to exert an influence on the incidence of dumping as a clinical problem.

Implantation of Radioactive Yttrium (Y^{90}) in the Sella Turcica for the Treatment of Carcinoma of the Breast and of the Prostate in the Advanced Stage: Considerations in 21 Cases. P. Goffrini, F. Fesani and A. Peracchia. Arch. ital. chir. 85:269-302 (no. 4) 1959 (In Italian) [Bologna, Italy].

Twenty-one patients with carcinoma in an advanced stage, including 15 women with carcinoma of the breast, with relapses or metastasis present in each case, and 6 men with carcinoma of the prostate, were treated by radiobiological destruction of the hypophysis by implantation of radioyttrium (Y^{90}) in the sella turcica. None of the patients had responded to previous roentgenotherapy or hormone therapy. Two days before the operation the patients were given antibiotics and balsamic preparations, parenterally or by inhalation, and 50 mg. of cortisone one hour before the operation; cortisone was continued postoperatively according to the clinical condition of each patient. Two tampons soaked in antibiotics were introduced into the nasal cavities a few hours before the operation; immediately before the operation they were replaced by 2 tampons soaked in a 1% epinephrine solution. All the patients were operated on under general anesthesia with endotracheal intubation and a pharyngeal tampon in order to prevent the descent of blood into the air passages and the digestive tract. Y^{90}, in the form of small bars, 4 mm. long and 1.3 mm. in diameter, was placed in the hypophysis by means of Greening and Stevenson's instrument, consisting of a needle-cannula, with a perforating needle, which was introduced through the nasal cavity and the sphenoid sinus, 2 to 3 mm. inside the anteroinferior surface of the sella turcica. The needle was then retracted, and the radioactive material was introduced into the cannula and pushed into the hypophysial tissue with a mandril. The Y^{90} used emanated beta radiations only with a maximum energy of 2.2 mev, the low power of penetration producing a well-localized necrosis. Each patient received 2 bars of Y^{90}, each of which had a minimal radioactivity of 4 mc.; in case of a lower charge, 3 bars were used. Histological observations made on 2 patients, who died on the 4th and the 60th day, respectively, after operation, showed that around each bar of radioactive material a zone of necrosis had formed, extending through the whole anterior lobe of the gland.

With the exception of one patient who died of a cerebrospinal fluid fistula 7 months after the operation, the operation caused no severe complications. Alterations of the eye movements, the most frequent complication observed, were not severe and were reversible. A subjective improvement was observed in 15 of the 21 patients, regression of the tumor in 8, and arrest of the tumor in 3. The subjective improvement, consisting of disappearance of pain and gradual improvement of the general condition of the patient, was not immediate. The authors believe that treatment with implantation of Y^{90} can be recommended because of the low incidence of trauma so far experienced with it and because it may offer a period of complete improvement in patients who no longer respond to any other treatment.

Reconstruction of the Bile Ducts: Hepaticointestinal Anastomosis with Transhepatic Insertion of a T-Tube. R. Muñoz. Rev. invest. clín. 11:217-223 (April-June) 1959 (In Spanish) [Mexico, D. F.].

In certain cases of cicatricial stenosis of the bile ducts, the distal segment of the common bile duct becomes atrophic and fibrotic. Reconstruction of permeability of the ducts by means of an end-to-end anastomosis is not possible. An anastomosis of the hepatic duct to the intestine makes it necessary to place a Y-tube within the anastomosis. This type of anastomosis often calls for a second operation, either to remove the tube obstructed with biliary sediment or to prevent stenosis from premature escape of the tube into the intestine.

A new technique has been used in the Hospital de Enfermedades de la Nutrición in Mexico City. The technique is described by illustrations. By this technique the hepatic duct is anastomosed to the intestine. A Cattell T-catheter maintains the permeability of the anastomosis, with the horizontal branch occupying the left hepatic duct and efferent loop of the intestine, and the vertical branch occupying the right hepatic duct and the liver. This technique was used in 4 patients. The period between the occurrence of the lesion in the bile ducts and the reconstruction varied between 4 months and 3 years. The catheter remained in place and permeable up to the period in which healing of the anastomosis was completed. It was managed in the usual form during the early and late postoperative periods, and was removed by traction at the end of 1 to 1½ years. The wound at the abdominal wall healed in 2 days. No complications occurred during the operation or at any time. A follow-up for 2 to 5 years has been proof of permanent satisfactory results.

Pure Ventricular Septal Defect and Ventricular Septal Defect with Pulmonic Stenosis: Hemodynamic and Clinical Changes Following Open Heart Surgery. V. Maranhao, G. T. Raber and H. Goldberg. Am. J. Cardiol. 4:155-162 (Aug.) 1959 [New York].

Preoperative and postoperative right heart catheterization and clinical evaluation were performed in 12 patients who underwent open-heart surgery. Seven had pure ventricular septal defects, while 5 had ventricular septal defect and pulmonic stenosis. In all the patients the pressures in the pulmonary artery and the right ventricle fell postoperatively, as did the pulmonic blood flow, the work of the right ventricle, and the total pulmonary vascular resistance, while the left ventricular work was increased. Physiologically and clinically, all the patients were improved in this selected series. In both groups a complete right bundle-branch block was observed after operation in the electrocardiogram and the vectorcardiogram.

The authors feel that the data they obtained indicate that a patient with a pure ventricular septal defect or ventricular septal defect with pulmonic stenosis, when well selected and well prepared for operation, can tolerate closure of the ventricular septal defect. The right bundle-branch block, which takes place postoperatively, perhaps is of no physiological importance. Open-heart surgery will be the procedure of choice for the majority of patients with these lesions.

Adrenalectomy in the Treatment of Metastases of Breast Cancer. J. A. Viaggio. Prensa méd. argent. 46:531-534 (Feb. 27) 1959 (In Spanish) [Buenos Aires].

Six patients with advanced forms of cancer of the breast, with metastases in the viscera and in either the bones or the lymph nodes or both, were operated on in the surgical department of the Hospital Pirovano of Buenos Aires between 1956 and 1959. The patients were between the ages of 38 and 66 years. Secretion of estrogenic substances was still active. All the patients had undergone a mastectomy during a period which varied from 7 months to 6 years before the appearance of the metastases. The second operation consisted of a bilateral oophorectomy followed by a bilateral adrenalectomy in 2 stages. The right adrenal was the first to be removed. Blood transfusion was given during the operation. Left adrenalectomy was followed by an intravenous infusion of levarterenol (Levophed) bitartrate in a 5% dextrose solution. The infusion was given at a rate of 20 drops a minute. After the operation cortisone and desoxycorticosterone acetate (DOCA) were given according to the following schedule: 1st day, 50 mg. of cortisone and 1 mg. of DOCA at 6-hour intervals; 2nd, 3rd, and 4th days, half the dose of each drug at the same time intervals. The maintenance treatment consisted of the daily administration of 50 mg. of cortisone in 2 doses of 25 mg. each.

A 3-year follow-up study showed that one patient died 10 days after the operation from acute tubular necrosis. In the remaining 5 patients the subjective and objective symptoms improved greatly. The secretion of estrogenic substances as well as pain had disappeared. Roentgenologic examination of the bone metastases showed calcification of the lesions. The lymph node metastases had regressed. The patients, previously bedridden, became able to walk. The appetite improved, and the patients gained some weight. In 2 of the patients the symptoms of cancer started to progress a few months after the operation, following periods of relief. At the end of the 3-year study, 3 patients were alive, with the objective and subjective symptoms under control. The author concludes that a bilateral oophorectomy, followed by either a unilateral or a bilateral adrenalectomy, is of great value as a palliative treatment of cancer of the breast. The satisfactory results will last so long as the sources of estrogen production, similar to those surgically removed, do not reappear.

Presence of Fungi in Gastric and Duodenal Ulcers. B. Holmström, S. Wallensten and A. Frisk. Acta chir. scandinav. 117:215-220 (no. 3) 1959 (In English) [Stockholm].

Specimens from the stomach and the duodenum of 30 patients undergoing gastric resection for ulcer or tumor were investigated for the presence of fungi. The patients were divided into 2 groups: Group 1 comprised 22 patients (10 with gastric and 12 with duodenal ulcer); group 2 comprised 8 patients (3 with no histological indication of ulcer, 2 with reepithelized ulcer, 2 with gastric carcinoma, and 1 with gastric neurofibroma). Samples were taken within a mean period of 3 or 4 hours after the operation, and secretion was taken from the ulcer crater or from the tumor, and also from the mucosa at approximately 5 cm. from the ulcer. Between 5 and 10 sections of each specimen were examined.

In group 1 the culture of samples was positive in 6 cases of gastric ulcer and in 6 of duodenal ulcer. The fungi types were identified as Candida albicans in 5 cases, Torulopsis glabrata in 4, C. tropicalis in one, Saccharomyces willianus in one, and both C. albicans and T. glabrata in one. The last 15 specimens in group 1 were examined concomitantly with culture of samples from the mucosa. This culture was positive in 5 instances. The growth was classified as plentiful in one specimen, as sparse in 3, and it showed one colony only in one case. The culture from the ulcer showed growth in all instances, except in the case with only one colony of fungi. Of the 22 patients with an "open ulcer," 12 who had been treated with internal medication were considered as having poor healing. Growth of fungi was demonstrated in ulcer samples from 7 of them. In relation to the 10 patients in whom the healing was not poor, the culture showed fungi in 5. Bacterial growth occurred in 10 patients (7 with gastric and 3 with duodenal ulcer), mostly of alpha and gamma streptococci.

In group 2 the fungous culture was negative in all the specimens, and there was growth of alpha streptococci in one. In the series as a whole, no specific histological features were observed in association with the presence of fungi. The infiltration of inflammatory cells varied from sparse to plentiful and was no more massive in the ulcers with positive culture than in the others. The fungi recovered in this study were saprophytes, although the majority were potential pathogens. It is possible that the fungi interfere with healing of the ulcer.

Serum Transaminase Activity as an Index of Liver Cell Destruction. G. Arturson and B. Persson. Acta chir. scandinav. 117:221-229 (no. 3) 1959 (In English) [Stockholm].

Determinations of serum glutamic oxalacetic transaminase (SGO-T) were performed on a single serum sample from each of 57 hospitalized patients suffering from various types of biliary tract disease. The diagnoses were verified mostly at operation or by autopsy. Tests of the liver function were also performed in combination with the SGO-T determination. Liver biopsy was performed on 15 patients. As the cephalin flocculation test, the thymol reaction, and the Takata reaction are positive only in cases of liver cirrhosis, it was considered valuable to compare the different levels of serum alkaline phosphatase and SGO-T in relation to the different types of disease involved in this study.

In patients with an uncomplicated gallstone condition, the values were normal for both enzymes, whereas in those with choledocholithiasis there was often an increase in the SGO-T level. This difference probably indicates that liver-cell destruction is more frequent and more pronounced when the gallstone disease is complicated by an infection of the bile ducts or by pancreatitis than in simple noninfectious bile duct disease. In patients with metastases in the liver, the serum alkaline phosphatase values were high, but the SGO-T activity was only slightly increased. The reverse was observed in patients with liver cirrhosis. In biliary obstruction the SGO-T levels were high, and the alkaline phosphatase levels only slightly increased when the obstruction was caused by gallstones; this relation was reversed when the obstruction was caused by cholangitis or by tumors of the bile ducts or of the pancreas. Even long after the elimination of the obstruction, there remained signs of liver-cell destruction. In all instances in which liver biopsy permitted comparison with histological aspects, increased SGO-T levels were found only in association with cell degeneration or actual necrosis.

The findings indicate that biliary obstruction caused by gallstones in the common bile duct leads to a more pronounced liver-cell damage than obstruction due to tumors. It seems justified to assume that an increased level of SGO-T suggests desintegration of the liver cells, although a normal level does not indicate a normal liver function. Even a single SGO-T determination, combined with liver function tests, can be a valuable index of acute liver-cell destruction. It seems especially useful for the differentiation of various types of biliary obstruction.

Hernias and Eventrations: Boiled Skin Graft. A. Dimopulos and J. O. Valenziano. Prensa méd. argent. 46:528-530 (Feb. 27) 1959 (In Spanish) [Buenos Aires].

Deep-skin transplantation involves occasional dangers of suppuration, rejection of the graft, pilocystic formations, and other complications. With the purpose of avoiding such complications, the authors and their associates used a boiled skin graft for the first time when, during a hernia operation, the skin flap was accidentally contaminated. The postoperative period was uneventful, and the transplantation had a satisfactory course. After this experimental use of boiled skin graft, 120 patients with hernias or eventrations were operated on according to the new technique. The most noticeable result has been the prevention of suppuration; in all 120 cases the graft has been firmly retained. As a rule, there is a light aseptic secretion from the drainage tubes which are systematically inserted.

Suppuration of subcutaneous tissue occurred in only one of the 120 patients, and even in this case the graft, firmly adherent under the surgical wound, was not eliminated. The suppuration was drained easily, and the wound healed by secondary intention. No pilocystic formation was observed.

While being boiled, the skin undergoes several changes. Macroscopically, the epidermis becomes easily detachable and 3 times as thick. It loses in length and becomes less resistant than when used "raw." After boiling 4 minutes, the dermis turns into a hyaline mass; and after 6 minutes, it is completely homogenized. The authors recommend the following steps: (1) shaving, washing, and scrubbing the area of operation, preferably in an isotonic sodium chloride solution; (2) painting the area with a 2% iodine tincture; (3) boiling the skin graft, extracted during the operation, 6 minutes in water which has been boiling 30 minutes; (4) rubbing the skin with gauze in order to remove all the epidermis; and (5) placing the graft, without any distention, on the area to be repaired, separate stitches being used at approximately 10-mm. distance. It is advisable to discard any portion of skin which presents several cicatrices. When there is only one scar, the skin can be used, provided that the scar remains in the middle of the graft. The author recommends that the technique of plastic surgery with boiled skin graft be extended to repairs of the face and breast.

Use of Teflon Mesh in the Repairs of Musculofascial Defects. L. G. Ludington and E. R. Woodward. Surgery 46:364-373 (Aug.) 1959 [St. Louis].

Teflon (polytetrafluorethylene) is one of the most inert plastics yet discovered. Its most unique characteristic is its nonwettability. It cannot be wet with water, and practically nothing will adhere to it. Its tenacity is 1.6 to 2.0 Gm. per denier; elongation at break is 15 to 33%; it is not affected by moisture, heat up to 400 to 500 F, or age; and it is inert to acids, alkalies, organic solvents, bacteria, and fungi. Implantation in body tissues up to one year reveals no loss of strength, while nylon loses about 80% of its strength due to hydrolysis and chemical deterioration. Teflon fabrics can be easily prepared for surgical use by washing in detergents to remove plasticizers and can be autoclaved as many times as necessary.

The authors used close, medium, and loosely woven Teflon fabrics to repair surgically created fascial defects in dogs. These experiments confirmed the highly inert nature of Teflon to animal tissues. Loose-weave Teflon fabrics proved superior, because they are quickly and completely incorporated with fibrous tissues, while the tightly woven fabrics tend to prevent this healing process. A new loose-weave fabric, especially woven to prevent fraying, was used. In case of infection, this loosely woven fabric with large interstices has a chance of maintaining itself without being extruded or forming a draining sinus, as long as cotton or silk sutures are not present. Rapid connective tissue growth about each Teflon thread isolates the graft from the infection, allowing the wound to heal.

From April 19, 1957, to Dec. 12, 1957, the authors used Teflon prostheses in 26 patients with difficult hernias, on the surgical service of the Wadsworth General Hospital at the Veterans Administration Center in Los Angeles. Of these patients, 13 had postoperative abdominal hernias, 4 of which had been repaired 2 or more times previously. There were 13 inguinal hernias, all of which were recurrent except in the case of one obese patient with bilateral direct and indirect hernias. There was also one large spigelian hernia and a recurrent femoral hernia. The patients have now been followed for from 6 to 12 months without recurrence of their hernias.

The authors feel that Teflon is a promising fascial substitute, superior to other plastic materials used heretofore, and it has many advantages over tantalum mesh. These advantages are its ease of handling, its availability and low cost as compared with tantalum, its proved strength in body tissues over long periods without chemical deterioration or fragmentation, and its inertness to body tissues which equals that of tantalum. In case of reoperation for other intra-abdominal conditions, Teflon need not be removed, as would be the case with tantalum, and it is nonopaque to x-rays.

Surgical Treatment of Ulcerative Colitis: A Comparison of Single-Stage Coloproctectomy with Other Procedures. C. W. McLenathen and J. A. Weinberg. Am. J. Surg. 98:165-174 (Aug.) 1959 [New York].

In order to assess the merits of several surgical methods of treatment of ulcerative colitis, the authors reviewed the results obtained in 42 patients with this disease, who were operated on at the Veterans Administration Hospital in Long Beach, Calif., between 1952 and 1959. The 42 patients were divided into 3 groups. The first group consisted of 26 patients who underwent initial procedures less radical than total coloproctectomy, such as simple ileostomy, ileoproctostomy, ileostomy and partial colectomy with establishment of a sigmoid fistula, colectomy and ileoproctostomy, and hemicolectomy with or without colostomy. Eighteen of these 26 patients had additional surgical procedures because of unsatisfactory results with the primary operations. Of the 8 patients who did not have secondary operations, 3 died of the disease. The 5 surviving patients in this group had severe postoperative disturbances, such as severe diarrhea, malnutrition, bleeding, and anal fistula formation. The second group consisted of 4 patients who underwent planned two-stage total coloproctectomy with ileostomy. The eventual results were satisfactory in all the patients, although disability was prolonged for several months in each of them because of the division of the operations into stages.

The third group consisted of 12 patients who underwent one-stage total coloproctectomy and ileostomy. There was one surgical death which occurred 3 days after an emergency operation for massive bleeding. The immediate cause of death was coronary vessel disease. With the exception of this patient, the results were uniformly satisfactory. There was early restoration of health and return to the former status of activity. The only significant postsurgical complications were several ileostomy disturbances which occurred in the first 7 patients who were operated on by means of a protruding type of ileostomy. This resulted in complications of prolapse in 2, stricture in 3, and fistulas in 2, which made surgical revision of the ileostomies necessary. In the past several years the flush type of ileostomy was used; there have been few complications, and most have required no more than minor procedures for their correction.

Total coloproctectomy is favored when ulcerative colitis becomes intolerable and is no longer responsive to medical management. Medical management should be continued as long as the patient is able to adjust himself to the disease. The one-stage procedure is favored over planned multiple stages for total resection with ileostomy, because it brings immediate relief to the patient without a prolonged convalescence in which complications may arise and in which the patient suffers economic loss. Surgical mortality does not appear to be a factor against the one-stage procedure. The immediate postoperative convalescence is more satisfactory than with multiple-stage procedures, probably because of the immediate and total removal of the source of toxic absorption. While multiple stages may give the patient an opportunity to adjust to the acceptance of permanent ileostomy during the weeks or months between stages, this is not to be considered an important enough consideration to weigh against the use of the one-stage procedure.

Postamputation Radiographic Evidence for Small Artery Obstruction in Arteriosclerosis. E. A. Edwards. Ann. Surg. 150:177-187 (Aug.) 1959 [Philadelphia].

In an attempt to determine the pattern of occlusion in the smaller vessels of the foot and toes of diabetic and nondiabetic patients with arteriosclerosis, the authors employed postamputation angiography in 13 arteriosclerotic lower extremities of 6 women and 7 men, between the ages of 57 and 89 years, with arteriosclerosis serious enough to lead to amputation. Four of the 13 patients had diabetes mellitus, while diabetes was ruled out in the other 9 patients by repeated blood and urine examinations. Four lower and 2 upper extremities of young patients were also studied with the same technique. These extremities were amputated for proximal nonvascular disease. Their vessels were presumably normal, and the angiograms offered confirmation of the pattern of arteriosclerotic occlusions. The smaller named and unnamed arteries of the foot were the sites of extensive occlusion in arteriosclerotic extremities which had been amputated. The arteries involved included the branches to both the medial and lateral parts of the heel, as well as the metatarsal arteries and those to the free borders of the 1st and 5th toes. The other digital arteries were less frequently diseased. There was no difference in the pattern of occlusion between the feet of patients with diabetes mellitus and those without diabetes. Occlusions were similarly as widespread in most of the patients without diabetes mellitus as in those with diabetes. In 2 of the 13 extremities the postamputation injection revealed arteriovenous shunting taking place at several sites in the tarsal area. It is not known whether this phenomenon existed in vivo.

Hypnosis as an Adjunct to Surgical Therapy. R. C. Doberneck, W. O. Griffen Jr., A. A. Papermaster and others. Surgery 46:299-304 (Aug.) 1959 [St. Louis].

The authors call attention to an earlier report on the successful use in their clinic (department of surgery, University of Minnesota, Minneapolis) of hypnosis in the treatment of the dumping syndrome after gastric resection for peptic ulcer (J. A. M. A. 165:1957 [Dec. 14] 1957). They continued the use of hypnosis in this entity, and also employed it in other conditions. To date they have used hypnosis in 105 patients, 99 of whom have been followed for at least 2 months. Thirty-two patients with severe symptoms of dumping after gastric resection have been treated with hypnosis, which is given initially once each week for approximately a month. No dietary restrictions are imposed during therapy, and, in fact, patients are encouraged to ingest previously offending foods. These patients have been followed up for an average of 14 months. Thirty of the 32 patients experienced symptomatic improvement, and 26 gained weight.

Thirty-one patients, undergoing cholecystectomy, colectomy, and gastrectomy for benign disease, were given hypnotherapy prior to their procedures. A control group of 31 patients was observed. The postoperative period was less difficult; there were less complaints; and the need for narcotics was less in the treated than in the control group.

The group treated with hypnosis for pain relief included 17 patients. Results were especially gratifying in the 4 patients with phantom limb syndrome and in the 3 with metastatic cancer. Eleven patients, who were previously on various dietary measures without success, were placed on reducing diets reinforced with hypnotic suggestion. Six of these patients refused to continue with the therapy and were considered failures. The other 5 patients have lost weight, and, most encouragingly, none of these 5 have regained any of the weight they lost. Hypnoanesthesia was used in an attempt to overcome the discomfort associated with minor surgical procedures and particularly endoscopic procedures. Of 8 patients who were hypnotized prior to proctoscopy, 7 experienced no discomfort.

The authors feel that hypnosis is a useful adjunct to surgery. It alloys the fears of the apprenhensive patient and removes the immediate and remote consequences of the surgical procedure. Willingness, as well as ability, to cooperate is a *sine qua non* for the success of hypnotherapy in any subject. Suggestions can be more easily imparted to patients in the hypnotic than in the waking state.

GYNECOLOGY & OBSTETRICS

Eugenic Interruption of Pregnancy Because of **Exposure to Ionizing Radiation.** H.-J. Maurer. Deutsche med. Wchnschr. 84:1336-1338 (July 24) 1959 (In German) [Stuttgart, Germany].

The author discusses the problem of the prophylactic interruption of pregnancy for eugenic reasons after exposure to ionizing radiations. A 25-year-old woman had requested interruption of her pregnancy, because intravenous pyelography, with 3 roentgenographic exposures, had been carried out at the beginning of the third month of gestation, and had disclosed a ureteral calculus. The radiobiological and ethical reasons for refusing the request for interruption of pregnancy are discussed. The author points out that the dose involved in the roentgenologic examination was small, and that normal children have been born to mothers who were exposed to therapeutic dosage, that is, much higher doses of radiation than are used in diagnostic procedures. He deplores the "irradiation phobia" now prevalent, and suggests that it is illogical to stress the possible mutagenic effect of ionizing radiation only, while completely disregarding the possible mutagenic effect of certain medicaments. He feels that in the future medicaments should be examined with regard to their genetic as well as their pharmacological effects.

The author does not wish to imply that, because of these added harmful effect of drugs and of certain natural irradiations, it is justifiable to disregard the possible harmful effects of ionizing radiation involved in diagnostic procedures. On the contrary, caution is necessary in roentgenologic studies, particularly in young persons and when the gonads are exposed.

Vaginal Trichomoniasis: Role of Trichomonas Vaginalis and of Candida Species in the Etiology of Leukorrhea. M. P. Barreto, H. Zago Filho, P. V. de Oliveira and others. Rev. Assoc. méd. brasil. 5:138-148 (April-June) 1959 (In Portuguese) [Sâu Paulo, Brazil].

In a series of 593 patients who were subjected to detailed gynecologic examination at the Mercy Hospital in Ribeirão Preto, Brazil, there were 486 (82%) with leukorrhea. Among the 252 women in this group who were pregnant, 215 (85.3%) had leukorrhea. This percentage is very close to the percentage found in the nonpregnant group (83.5%), which shows the absence of any statistically significant difference between the 2 groups. Vaginitis was present in 193 patients (32%), with or without cervicitis or vulvitis. Cervicitis was found in 365 subjects (61.6%), with or without other lesions. Leukorrhea was associated with vaginal or/and cervical lesions in 414 patients (85.2%). Trichomonas vaginalis was present in 195 (approximately 40%), and Candida organisms in 72 (14.8%) of the

486 women with leukorrhea, while 37 (7.6%) had both T. vaginalis and Candida organisms. These frequencies mean that either T. vaginalis or a Candida species, or both, were present in 58% of the patients with leukorrhea. The finding is inconclusive as to the etiological role of these parasites in the frequency of leukorrhea in either pregnant or nonpregnant women.

Among the 232 patients with trichomoniasis, there were 159 cases (68.5%) of cervical lesions, with or without vaginal lesions. There were also 206 patients (approximately 80%) with vaginal or/and cervical lesions in the group of 254 patients without trichomoniasis. This finding indicates a negative correlation between T. vaginalis and vaginal or cervical lesions. Among the 72 patients with leukorrhea in whom only Candida species had been found, 6 had also vaginitis, 19 had cervicitis, and 29 had both types of lesion. The data collected in this series show that T. vaginalis and a Candida species can be present and multiply in the vagina without causing visible lesions. The association of vaginitis and/or cervicitis with these vaginal parasites may be only coincidental.

A Clinicopathologic Study of 172 Patients with Primary Carcinoma of the Ovary. J. C. Turner Jr., W. H. ReMine and M. B. Dockerty. Surg. Gynec. & Obst. 109:198-206 (Aug.) 1959 [Chicago].

The authors evaluate the results of surgical treatment in patients with primary carcinoma of the ovary, observed at the Mayo Clinic during the years from 1945 through 1949. The diagnosis of carcinoma was proved by multiple histological sections. The clinical data as well as the pathological material were reviewed in every patient. Cases of metastatic (secondary) carcinoma of the ovary were excluded, as were those of functioning ovarian tumors, such as granulosa-cell tumors, arrhenoblastomas, and dysgerminomas. Cases in which the primary operation was not performed at the clinic were likewise excluded. During the 5-year period covered by this study, 172 cases met the aforementioned requirements, and these comprise the basis of this study. The peak age incidence was in the 6th decade, and the commonest symptoms were abdominal pain and swelling.

The relative over-all 5-year survival rate was 54.3%. When the papillary serous cystadenocarcinomas were excluded from the analysis, the over-all 5-year survival rate was 49.4%. Prognosis depended chiefly on the histological type of tumor and on the histological degree of malignancy, both of which control to a large degree the clinical extent of the disease. Patients with ovarian tumors of low-grade malignancy have the most favorable prognosis (82.8% of 5-year survival rate for patients having grade 1 malignant lesions). Similarly, tumors confined to the adnexa react most favorably to treatment. The clinical extent of the disease at the time of exploration seems to be the determining factor in survival when the cystic component of the ovarian carcinoma is ruptured at the time of surgical removal. A tabulation of results obtained in patients treated by operation alone, compared with those who received additional radiation therapy, is in no way indicative of the value of irradiation, because the patients with the poorest prognosis were the ones receiving this additional therapy. Yet the authors believe that radiation therapy has a definite place in the treatment of patients with ovarian cancer of advanced grades, chiefly to prolong survival time and perhaps, occasionally, to cure residual disease.

Childbirth After Pneumonectomy. H. F. R. Plass. Minnesota Med. 42:1099-1100 (Aug.) 1959 [St. Paul].

The author reports 2 cases of young women who became pregnant and had uneventful deliveries after the removal of one lung because of bronchiectasis. The first patient continued to have productive cough and hemorrhage after the removal of her right middle and lower lobes. These symptoms led to the removal of the remaining portion of the right lung 4 years later. After this operation there was marked herniation of the left lung into the right chest cavity through the superior mediastinum. The patient had precordial pain, dyspnea, and numbness in the left arm for about a year. Two years after the last lung operation she became pregnant. She was then 29 years old, and her general condition seemed improved. There was no rise in the normal venous pressure and no change in the breathing capacity. During the pregnancy there was total relief from all the symptoms related to her shifted mediastinum. The delivery was normal, and the patient had no other major illnesses during the following 12 years, except for 3 attacks of pneumonia in the left lower lobe.

The second patient was first seen by the author when she was an unmarried 20-year-old, and had already had the lower left lobe and the lingula removed after a long history of bronchiectasis. As she continued to have fever bouts associated with increased amounts of sputum, removal of the remaining portion of the left lung and thoracoplasty were performed. After a 2-month period of remission, her symptoms recurred and were further complicated. Five years after she was first seen by the author, the diagnoses were absent left lung, bronchiectasis and emphysema of the right lung, mitral stenosis, chronic pansinusitis, hay fever, asthma, and migraine. The patient was married 2 years later and became pregnant. At delivery her vital capacity had remained unchanged (2 liters), and her pulse had risen to 120 at rest. There were no other signs of pulmonary or cardiac distress. Delivery was easily accomplished by cesarean section under local anesthesia, at 36 weeks of pregnancy. During the year after the delivery the patient had an attack of sinusitis and otitis, which was cured with penicillin and sulfadiazine. She continued with desensitization therapy and had only minor asthma and hay fever.

Incomplete Abortion: Contribution to Its Therapy. P. L. Froldi. Hospital 56:89-92 (July) 1959 (In Portuguese) [Rio de Janeiro].

The author reports on 140 cases of incomplete abortion, of which 128 were observed on the gynecologic service of the Mercy Hospital, and 12 at the Emergency Hospital in Rio de Janeiro. The series was divided into 3 groups: Group 1 consisted of 34 patients with profuse hemorrhage; group 2, of 11 patients with fever; and group 3, of 95 patients without any complication. The patients in the first group were treated surgically by immediate uterine curettage. Those in groups 2 and 3 were treated conservatively, i. e., they were given a treatment aiming at evacuation of the uterus by medication. This conservative treatment consisted in the preliminary administration of an aqueous solution of folliculin, followed one hour later by the administration of combined quinine and Cardiazol in the form of tablets. Each patient received one tablet (containing 0.10 mg. of quinine) every half hour until a total dose of 6 tablets was reached. One hour after the administration of the last tablet, 2 units of posterior pituitary preparation was injected. If necessary, the whole treatment was repeated during 3 days.

Of the 11 patients who had fever, 7 had complete uterine evacuation as a result of the quinine-Cardiazol therapy. The other 4 underwent uterine curettage after 3 days of unsuccessful medical treatment. Their general condition was much improved, and they had become apyretic during the conservative therapy. Of the 95 patients who had uncomplicated incomplete abortion, 83 (63%) eliminated their ovular remainders within 1 to 3 days of treatment. The other 12 (37%) eventually underwent uterine curettage. Taking the series as a whole, the conservative treatment was successful in 90 (86%) of the 106 patients to whom it was applied, with complete recovery within 5 days. In the 16 patients who eventually needed to undergo uterine curettage, the medical therapy was instrumental in suppressing or avoiding infection and in improving the general condition.

Use of Selected Useful Rauwolfia Alkaloids in the Dilatation of the Uterine Cervix in Labor. N. E. Vie and F. G. Mariona. Semana méd. 66:60-66 (July 9) 1959 (In Spanish) [Buenos Aires].

The effects of a mixture of Rauwolfia alkaloids on the speed and mechanism of the passive phase of uterine dilatation during labor were studied by the authors in 50 patients admitted to the obstetrics service of San Isidro Maternity Hospital in Buenos Aires. There were 23 primiparas, 10 secundiparas, and 17 multiparas. There was a great variation as to age, type of presentation, and condition of the membranes. The preparation used was an injectable solution of selected Rauwolfia alkaloids, free from any possible secondary effects; it was packaged in ampuls containing 1 mg. of the drug dissolved in an aqueous vehicle. The solution was injected intramuscularly as soon as a cervical dilatation of 2 cm. was reached. If necessary, a second injection was given. No other sedative, antispasmodic, or oxytocic medication was allowed.

The average duration of labor was 12 hours for the primiparas and 8 hours for the secundiparas and multiparas, as compared with the accepted averages of 15 hours for primiparas and 10 to 12 hours for multiparas. The delivery was spontaneous in 31 patients (62%). In 19 (38%) the use of the Credé method of placental removal was necessary. Four patients (8%) had a forceps delivery, due to insufficient dilatation or rotation, or because of fatigue of the patient. There was no fetal mortality. Comparing the amount of dilatation before and after the injection of the Rauwolfia alkaloid mixture, it was found that in the majority of the patients there was a minimum of dilatation corresponding to a larger percentage of the total time of labor in the preinjection period. In the postinjection period there was a noticeable acceleration of the dilatation process, manifested in a greater amount of dilatation accomplished during a lower percentage of the total duration of labor.

No significant changes were observed in the dynamics of labor, although there was a tendency toward uniformization of the uterine contractions, which helped speed the labor mechanism. A high percentage of the patients remained in a state of calm expectation and thus contributed to an easier conduct on the part of the obstetrician. Normotensive patients experienced no blood pressure alterations. In those with a systolic pressure above 135 mm. Hg, there was a fall of up to 20 mm., while the diastolic pressure remained unchanged, except in one patient in whom it dropped in the same proportion as the systolic.

PEDIATRICS

The Absent Spleen Syndrome. D. W. Polhemus and W. B. Schafer. Pediatrics 24:254-257 (Aug.) 1959 [Springfield, Ill.].

The authors report on a newborn female infant in whom the correct diagnosis of absent spleen syndrome was made before death. This infant who exhibited intermittent cyanosis from birth was admitted to Childrens Hospital, Los Angeles, at the age of 2 days. Auscultation revealed a harsh, grade 3 systolic murmur, loudest over the lower part of the sternum. The inferior edge of the liver was palpable 1.5 cm. below the right costal margin and 2 cm. below the left costal margin and was initially thought to be the spleen. The concentration of hemoglobin was 23.1 Gm. per 100 cc., and the leukocyte count was 19,800 per cubic millimeter, with 64% granulocytes, 21% lymphocytes, 14% monocytes, and 1% eosinophils. A few Howell-Jolly bodies and occasional target cells were noted. There were 1 or 2 normoblasts per 100 leukocytes. Methyl violet stain revealed many Heinz bodies. Fluoroscopic studies demonstrated decreased pulmonary vasculature, a narrow base of the heart without cardiac enlargement, and dextroposition of the stomach which led to the diagnosis of absent spleen syndrome. The electrocardiogram was suggestive of left ventricular hypertrophy. Bone marrow examination revealed normal findings, and also electrophoresis of the serum showed a normal pattern of proteins.

Five weeks later the infant manifested dietary difficulties, irregular respiration, and a bulging anterior fontanel. Urinanalysis revealed 3 plus reaction for albumin and many microscopic leukocytes and bacteria. Cultures of the urine yielded Escherichia coli. The leukocyte count in the cerebrospinal fluid was 600 per cubic millimeter with 68% granulocytes. Cultures of the cerebrospinal fluid and blood were negative. Roentgenograms of the chest showed cardiomegaly and pulmonary congestion. Although meningitis was apparently present, it was atypical. The infant's condition rapidly deteriorated despite therapy, and she died at the age of 6 weeks. Autopsy showed the congenital absence of the spleen with atrioventricular communis and partial transposition of the abdominal viscera.

It is apparent that in all cases of undiagnosed cyanotic heart disease of infancy appropriate hematological studies should be carried out. Abnormalities of the peripheral blood indicative of absence of the spleen are highly suggestive that the complete syndrome is present. When fluoroscopic examination also demonstrates a transposed stomach, the diagnosis is certain. Improvement in surgical techniques will, it is hoped, permit correction of these cardiac defects, thus increasing the diagnostic value of hematological studies of the kind described.

An Observation of Congenital Galactosemia: Evolution of the Hepatic Lesions: Evidence of Enzymatic Deficiency: A Familial Study. R. Joseph, M. Ribierre, J. Job and others. Semaine hôp. Paris 35:2107-2115 (June-July) 1959 (In French) [Paris].

An observation of congenital galactosemia in a 3-month-old boy with neonatal icterus and denutrition is presented. His clinical signs and symptoms—jaundice, ascitic cirrhosis with voluminous hepatomegaly, light albuminuria, melituria, and incipient bilateral cataract—proved to be characteristic of galactosemia. The diagnosis was confirmed by the finding of sugar in the urine and later by the discovery of the enzymatic deficiency which is the cause of the disease. Use of the technique of Kalckar permits sure diagnosis of galactosemia, and through it the disease can be detected at an early stage. In the patient discussed, a milkless diet was introduced at the age of 3 months, and under this diet the hepatic symptoms and the cataract showed rapid regression. The child's psychomotor development, however, was slightly retarded.

Histological study of this case was complete, and the regression of the hepatic lesions is described in detail. Four puncture biopsies of the liver were performed during the first 14 months after omission of milk from the diet. At the last biopsy the hepatic cells were perfectly normal, and there was a large oversupply of glycogen. There was no Kupffer cell hyperplasia and no fibrillary reticulosis. Quantitative determination of the galactose-1-phosphate-uridyl transferase in the patient's red blood cells by means of Kalckar's method showed a complete absence of this enzymatic activity. Results of the Kalckar test in the child's parents were normal; however, the provoked galactosemia test had abnormal results in his brother and slightly disturbed results in his sister. Another member of the family had died at the age of 12 days of an icterus gravis which was probably of galactosemic origin.

DERMATOLOGY

Griseofulvin, a New Oral Antibiotic for the Treatment of Fungus Infections of the Skin. A. Flint, R. R. Forsey and B. Usher. Canad. M. A. J. 81:173-175 (Aug. 1) 1959 [Toronto].

The authors used griseofulvin, a new oral antifungal agent in the treatment of 9 patients with ringworm infections involving the nails, the scalp, and the skin. Griseofulvin was given in doses of 250 mg. 4 times a day for periods ranging from 2 to 4 weeks in patients with scalp infections, and the same amount but for periods ranging from 4 to 6 months in those with infection of the nails. This drug has proved to be highly effective in infections caused by Microsporum fungi, and it has been particularly valuable in treating stubborn cases of tinea unguium and infections with Trichophyton rubrum previously resistant to all types of treatment. While this drug is effective in all superficial cutaneous mycoses, the results obtained in patients with nail infections were particularly striking. The only side-effects noted were mild gastrointestinal discomfort and headache, which subsided despite continuation of therapy. The advent of this effective antifungal agent will contribute toward eradication of epidemics caused by ringworm in man as well as in domestic animals; but because of its low toxicity, the indiscriminate use of griseofulvin could lead to resistant strains. It is advisable, therefore, to limit its use to cases of ringworm infection in which diagnosis has been correctly made and established by cultures.

Treatment of Acne Vulgaris with Polythionates Incorporated in a Vanishing Cream Vehicle. J. R. Delaney, R. J. Ferrara and I. Robarge. J. Michigan M. Soc. 58:1259-1261 and 1278 (Aug.) 1959 [St. Paul].

The authors evaluated the therapeutic efficiency of 2 proprietary preparations of polythionic acid salts, Dermasulf and Topisulph, in a vanishing cream vehicle. Seventy-two patients with mild acne to severe cystic acne were treated with one or the other test preparation. The ages of the patients ranged from 11 to 35 years, and there were more female than male patients. About 40% of the patients had at some time been given other therapy for their condition. The duration of the disease had ranged from 2 months to 20 years. All the patients presented facial lesions to a greater or less extent. In some, the involvement extended to the presternal, scapular, shoulder, or back areas. Dermasulf or Topisulph was applied 2 or 3 times daily, depending on the oiliness of the skin of the individual patient. Treatment periods varied in length from 2 weeks to 15 months, contingent on the severity of the condition treated and the response to therapy.

Dermasulf and Topisulph in their vanishing cream vehicles elicited quite comparable responses. Their effectiveness was equally apparent in those patients receiving an initial course of therapy and in those who had undergone other therapies previously. Dermasulf yielded "good" or "excellent" results in 69% of the subjects using it and "fair" results in 24%. Topisulph produced "good" or "excellent" results in 67% of the patients and "fair" results in 27%. About 7% of the patients in either group responded poorly to the polythionate preparations. In no instance were untoward reactions encountered, nor was rejection of the medication made for any reason by any of the participants in the study. Both preparations were found to be esthetically appealing. This study demonstrates that the polythionates are an effective topical adjunct in the control of acne vulgaris. It is suggested that Dermasulf in a vanishing cream base provides the physician with an alternate dosage form to Dermasulf liquid, which should logically extend the clinical usefulness of this product.

Premature Canities, Calvities and Migraine. E. B. H. De Haas. Nederl. tijdschr. geneesk. 103:1425-1427 (July 11) 1959 (In Dutch) [Amsterdam].

The author had long been under the impression that patients subject to attacks of migraine frequently had a tendency to premature grayness (canities) or baldness (calvities), and that often these anomalies also occurred in their families. He was surprised that he was unable to find literature reports on this problem, and that no mention was made of it in family histories of migraine patients. He presents the case histories and family trees of 2 patients who, in addition, had an obstruction of the retinal artery. Patient A had been subject since youth to attacks of migraine which began with a flimmer scotoma. At the age of 23 a persisting scotoma suddenly developed in her left eye. This was caused by closure of a cilioretinal artery, and could not be counteracted by vasodilator agents. In addition to migraine the patient complained of "dead fingers," of cramp-like pains in heels and toes, of intolerance for certain foods, and she became gray at the age of 30. Several members of her family had the same complaint.

In patient B the central retinal artery of the left eye was obstructed. Although this patient had not been troubled with headaches, he often had "dead fingers" and paresthesias in the finger tips; he had begun to become bald at the age of 22, and the remaining hair became gray at 35. His brother had migraine with flimmer scotoma and also premature calvities and canities. Female members of his family had premature canities (onset of grayness before the age of 30). Angiospastic and allergic disorders were also found in members of this family. It is suggested that anomalies of the pilous system may be the expression of a type of constitution which is also characterized by abnormal reactions and enhanced vulnerability of the diencephalon.

UROLOGY

Management of Early Prostatic Carcinoma. R. W. Barnes and D. S. Emery. California Med. 91:57-61 (Aug.) 1959 [San Francisco].

The successful control of prostatic carcinoma depends to a large extent on early diagnosis and treatment. The screening test for early diagnosis is palpation of the prostate through the anterior rectal wall. The best method of confirming the diagnosis is by open perineal biopsy or by the newer approach of transrectal needle biopsy. Open perineal exposure and removal of the nodule, together with other sections, from the gland is undoubtedly an accurate method, but transrectal needle biopsy offers more promise of accuracy than does perineal needle biopsy, is simpler to perform, and can be carried out as an office procedure. The authors performed 20 transrectal needle biopsies without any complications, except elevation of temperature for 2 days in 2 patients. There have been a few complications, however, in patients in whom open transrectal biopsy was performed, and the procedure required hospitalization for from 1 to 6 days. Cytological study of prostatic fluid has not proved to be of definite value in making a positive diagnosis of prostatic carcinoma. Serum acid phosphatase determination is of no value for diagnosis in the early stages of this disease.

Ten-year survival with conservative therapy, as determined in a review of 38 patients who were observed for 10 years or longer, was 50%. This survival rate compares favorably with the best reported in the literature after radical prostatectomy.

However, there was clinical evidence of the presence of carcinoma at the time of follow-up in 27 of the 38 patients in this series, whereas those patients on whom radical prostatectomy was performed were clinically free of cancer at the time of the last follow-up. Radical prostatectomy is indicated in the following patients: (1) those who have a life expectancy of more than 10 years; (2) those who represent an excellent surgical risk; and (3) those in whom the neoplasm is confined within the capsule of the prostate. Endocrine therapy is indicated when those criteria are not met. The results from endocrine therapy, when begun immediately after diagnosis, are significantly better than those from delayed treatment. Orchiectomy and the administration of estrogens promise a little longer survival than estrogens alone do.

Increasing Frequency of Recurrence of Gonorrhea after Penicillin Treatment (Same Preparation, Same Dose). H. C. Gjessing. Tidsskr. norske laegefor. 79:829-831 (July 1) 1959 (In Norwegian) [Oslo].

To determine the effectiveness of penicillin in the treatment of gonorrhea, it is important to distinguish between recurrence and reinfection. Recurrence is, as a rule, demonstrable 1 or 2 weeks after ended treatment. Reinfection is not due to ineffective treatment. Suspicion of reinfection increases proportionately with the gonococcus-free period between ended treatment and the new outbreak of the disease. The cause of unsuccessful treatment must be looked for in one or more of these categories: the patient, the medicament, the gonococcus. The author's impression is that alcohol, even in small amounts, up to a week after treatment, favors recurrence, and use of any form of alcohol during the first week after treatment is forbidden. A patient repeatedly treated with penicillin should not have a poorer chance for cure than one treated for the first time. At present there is no indication that the increasing tendency to recurrence is attributable to factors in the human organism, and it is not believed to be attributable to change of preparation. The third factor is the gonococcus.

The general conception today is that the increasing incidence of recurrence of gonorrhea is due to the development of gonococcic strains relatively resistant to penicillin. However, there are cases in which the bacteriological examination has shown a relative increase in resistance but a comparatively small penicillin dosage has effected cure. Since January, 1958, an injection of 600,000 units of procaine penicillin has been the standard treatment for men; since September, 1958, determination of penicillin resistance has been made before treatment. Preliminary reports show that up to May, 1959, 255 patients were treated, with 5 recurrences and 4 reinfections. There is no indication now for abandoning penicillin, as the main agent in the treatment of gonorrhea, in favor of streptomycin, as use of the latter has also been followed by rapidly increasing frequency of recurrence. Application of preparations containing both penicillin and streptomycin is not advised, since in case of recurrence it is not known to which substance the gonococci are resistant.

Transurethral Resection in Hyperplasia of the Prostate. W. Mathisen. Tidsskr. norske laegefor. 79:819-824 (July 1) 1959 (In Norwegian) [Oslo].

Transurethral resection has an important place in the treatment of prostatic hyperplasia, also of other prostatic and bladder diseases. When adequately performed, the method offers many advantages. It can be applied without great risk in patients whose general condition is rather poor and who are advanced in age. The late results are as good after transurethral resection as after any of the open methods. The procedure is technically difficult and requires practice and experience. The results will therefore depend not so much on the size of the prostate as on the manner in which the resection is performed.

OTOLARYNGOLOGY

Tonsillectomy and Allergy. M. F. Lerner and H. Markow. New York J. Med. 59:2888-2891 (Aug. 1) 1959 [New York].

The authors analyzed the histories of 70 allergic patients who had been attending the allergy clinic of the Beth-El Hospital in Brooklyn, N. Y., for the treatment of various types of allergies for the past 5 years. All the patients had had tonsillectomies performed at some time prior to admission to the clinic. Fifty of these patients manifested some type of allergy prior to surgery, and 20 were clinically nonallergic prior to tonsillectomy. Only 2 of the 50 allergic patients showed improvement after surgery, and those 2 were under continuous treatment for allergy prior to and after tonsillectomy. Seven patients showed improvement for some time after surgery, but symptoms recurred within 2 to 4 years postoperatively. In 16 of the remaining 41 patients no change could be observed; 8 of the patients were worse; and in 17 additional forms of allergy developed. Of the 70 patients in this series, asthma developed in 16 after tonsillectomy, and 13 patients who had asthma prior to surgery were unchanged postoperatively.

Asthma and nasal allergy per se are no indications for tonsillectomy. It may, on the contrary, induce new allergic manifestations in patients who are already allergic. The continued presence of neutrophils in the respiratory secretions is indicative of an infective process alone or superimposed on an allergic reaction of the tissues. The greater the eosinophilia in these secretions, the greater the possibility that one is dealing with an allergic reaction, and surgery should not be done, or should be postponed, until the allergy is under control.

Primary Diphtheritic Otitis Media: Review of the Literature and Report of a Case. J. J. Downes. A. M. A. Arch. Otolarygn. 70:27-31 (July) 1959 [Chicago].

Reviewing the literature on primary diphtheritic otitis media since 1925, when the last comprehensive study was published, the author found that 22 cases had been reported in the American and English literatures; 17 of these were described in detail. A case of otitis media was classified as primary diphtheritic on the basis of the following criteria: 1. The middle ear was the site of the major pathology. 2. A positive culture for Corynebacterium diphtheriae was obtained from the aural discharge. 3. Nasopharyngeal cultures, when obtained, were negative at the time of the first positive ear culture. In some instances nasopharyngeal cultures later were positive.

The age range of the patients whose case histories are reviewed was from 9 months to 38 years, but 75% were under 6 years. The only clinical evidence which may suggest aural diphtheria is the membrane formation on the tympanum or in the external canal. However, this membrane was found in only 23% of the cases. An aural discharge, which gave a positive culture for C. diphtheriae, was found in every case. Differentiation from diphtheroids was made on the basis of staining and morphologic characteristics and in some cases by guinea pig virulence tests. Pure cultures were obtained in all but 2 cases; the response to antitoxin in both of these instances proved C. diphtheriae to be the primary etiological organism. Acute mastoiditis was diagnosed in 35% of the cases; one case of chronic mastoiditis was described. Three cases, none of which had nasopharyngeal involvement, exhibited profound toxicity. The most important factor in the management of all the cases was the use of diphtheria antitoxin. Myringotomy was performed in 8, and mastoidectomy in 2 of the cases described. Signs and symptoms usually subsided within 3 weeks, and all the patients recovered without major sequelae. When the aural carrier state developed, its eradication was most readily accomplished (as with other carrier forms) by antibiotic therapy.

The case recently observed by the author concerned a 21-year-old American Indian woman, 34 weeks pregnant. Examination of the left ear revealed copious gray-white purulent exudate in the external canal. The drum was bulging and inflamed. A sample of exudate was obtained from close to the tympanum and streaked on Loeffler's medium. The patient was given benzathine penicillin G, 1,200,000 units intramuscularly. Oral administration of trisulfapyrimidines (triple sulfonamides) and an otic solution of sulfanilamide with urea and chlorobutanol were prescribed. The laboratory later reported that the culture had yielded a pure growth of C. diphtheriae. The patient could not be contacted until 6 days after the initial visit. At this time she stated that the external discharge had ceased 2 days previously. Diphtheria antitoxin (20,000 units) and diphtheria-tetanus toxoid (0.5 cc.) were given intramuscularly in separate sites. Nasopharyngeal cultures from members of the family and other contacts were all negative. Follow-up included cultures at 2-month intervals for 8 months. There has been no evidence to suggest a carrier state. In an addendum the author states that recently 3 additional cases of suppurative otitis media in infants yielding a pure culture of virulent C. diphtheriae have been diagnosed and successfully treated.

THERAPEUTICS

Hydrochlorothiazide in the Treatment of Chronic Heart Disease and in Other Hydrophilic Conditions. C. H. Keller. Deutsche med. Wchnschr. 84:1232-1236 (July 3) 1959 (In German) [Stuttgart, Germany].

Hydrochlorothiazide is closely related to chlorothiazide, differing from it only in that the heterocyclic portion of the ring is hydrogenated. The author used hydrochlorothiazide in 54 patients, 31 of whom had cardiovascular disturbances, mostly coronary sclerosis and hypertension. The remaining 23 patients had a tendency to water retention, although they did not actually have circulatory decompensation; most of them were obese. Two different procedures were used in the clinical evaluation. In the acute experiment the patients were given a single dose of 100 mg. of hydrochlorothiazide. This mode of administration demonstrates the diuretic effect, and permits the pharmacodynamic evaluation of the drug. The second method of evaluation, the long-term treatment, demonstrates the clinical value, and helps to decide whether intermittent or continuous administration is best.

The author found that hydrochlorothiazide is a very potent diuretic. The administration of 100 mg. of this substance doubled the amount of urine, multiplied the excretion of sodium and chloride, but had little effect on the potassium excretion. Restriction of sodium chloride in the diet had little added effect on the sodium excretion. In treating patients with chronic heart disease, who have a tendency to fluid retention, hydrochlorothiazide can be given in addition to the cardiac glycosides. Because of its almost inexhaustible diuretic effect, the drug permits a relaxation of salt restriction in the diet. In patients with obesity, who have a tendency to water and salt retention, hydrochlorothiazide produces a maximal weight reduction, but a restricted salt diet must be continued.

Treatment with hydrochlorothiazide should begin with a dose of 75 or 100 mg. on the first day. If continued medication is decided on, the dose can be reduced to 50 mg. during the following days. After the desired effect has been achieved, the dose can be reduced to 25 mg. For intermittent medication the author recommends a dose of 75 or 100 mg. once or twice weekly, in tablet form. A fruit diet is recommended for the day after the administration of the tablets. Since the diuresis usually persists for from 6 to 8 hours, the tablets should be given in the morning so as not to interfere with sleep at night. To counteract the tendency to hypopotassemia likely to result from hydrochlorothiazide medication, the author recommends the prophylactic administration of potassium chloride or the eating of dried apricots, which are rich in potassium salts.

The Treatment of Scleroderma with the New Chelating Agent, Edathamil. S. A. Muller, L. A. Brunsting and R. K. Winkelmann. A. M. A. Arch. Dermat. 80:187-194 (Aug.) 1959 [Chicago].

The authors report on 23 patients, between the ages of 12 and 67 years, with scleroderma of varying degrees, who were hospitalized at the Mayo Clinic and were treated with edathamil disodium, the disodium salt of ethylenediaminetetraacetic acid, a potent chelating agent. The drug was dissolved in 500 cc. of 5% dextrose in water or isotonic sodium chloride solution, and usually a daily dose of 3 Gm. was given intravenously in about 4 hours. Of the 23 patients, 20 had acrosclerosis, 2 had diffuse scleroderma, and 1 had widespread morphea. The course of treatment extended over a 3-week period. Three patients were given a second course of edathamil after an interval of 6 to 8 weeks. Significant improvement was noted objectively in 9 of the 23 patients, as measured by functional performance tests, esophageal motility studies, and over-all clinical evaluation. In 2 patients marked improvement continued for several months. The 3 patients who had a second course of treatment with edathamil showed no further change. The commonest complication of treatment with edathamil was burning at the infusion site, but ordinarily the burning pain was relieved promptly by slowing of the rate of infusion. The only significant complication was renal irritation; mild albuminuria occurred in the last few days of treatment in 6 patients, but was of no consequence. Severe albuminuria and a transient mild increase in blood urea necessitated the withdrawal of the drug in one patient after the administration of a total dose of 37 Gm. in a 13-day period.

Edathamil is a relatively safe drug to administer by intravenous drip. Some degree of renal irritation should be anticipated, although at the dosage recommended by Foreman and associates, i. e., 50 mg. of edathamil per kilogram of body weight daily for 5 days, followed by a 2-day rest period before repetition of the dose (J. A. M. A. **160**:1042 [March 24] 1956), it should be infrequent. At the present time, in the absence of any specific therapeutic agent in scleroderma, the use of edathamil in the systemic forms of scleroderma seems justified. The ultimate usefulness of this drug in the treatment of scleroderma awaits further evaluation.

The Clinical Response to Achromycin V (Lederle) in Infectious Diseases, and in Postoperative Complications of an Infectious Nature: Study of Its Nature in 27 Cases. R. Rodriquez-Molina, R. Menendez-Corrada, L. A. Passalacqua and M. I. Nickle. Bol. Asoc. méd. Puerto Rico 51:196-204 (June) 1959 (In English) [Santurce, Puerto Rico].

The authors report on the results of Achromycin V therapy in 27 patients for whom there were complete records and who had been selected from a larger series treated at the San Patricio VA Hospital in San Juan, Puerto Rico. Achromycin V contains 380 mg. of sodium metaphosphate to 250 mg. of tetracycline in each capsule; it appears in blood and urine more rapidly and at higher levels than tetracycline administered alone. The addition of sodium metaphosphate is credited with increasing the intensity and speed of the antibiotic action.

The 27 patients in this series fell into 2 categories: cases of possible infectious diseases, whether or not proved bacteriologically, and cases in which it is desirable to prevent secondary infection, as in surgical conditions. There were 3 patients with intestinal disorders, including 1 with bacillary dysentery; 9 with respiratory disease; 4 with genitourinary infection and positive urine culture; 7 with miscellaneous infections; 3 postoperative patients; and 1 with burns. The average dose of Achromycin V administered was 250 mg. every 4 to 6 hours. The results were considered excellent in 10 patients, good in 11, fair in 2, and poor in 3; in only one patient, suffering from diarrhea without any bacterial or parasitic findings, was there no response to the treatment. The results were evaluated in terms of the degree and rapidity of effects on the fever, the pathogenic bacteria, and the patient's general condition. The best results were obtained in patients with definite infectious diseases, such as abscesses and skin infections.

Treatment of Advanced Breast Cancer with Fluoxymesterone (Halotestin). V. L. Beckett and M. J. Brennan. Surg. Gynec. & Obst. 109:235-239 (Aug.) 1959 [Chicago].

This report concerns observations on 23 patients with metastatic carcinoma of the breast, who were treated with the orally administered androgen, fluoxymesterone (Halotestin). The patients were treated between January, 1956, and May, 1958, in the oncology division of the Henry Ford Hospital, Detroit. In 20 patients the diagnosis had been made at the time of mastectomy, and in 2 from tissue examination of metastatic lesions. In the one instance of no histological verification, there was the obvious history of an enlarging lump in the breast for 2 years, with subsequent appearance of skin nodules and enlarged lymph nodes. All except 3 of the women had undergone some form of mastectomy as the initial treatment. Two of the remaining 3 had been given x-ray treatment to the breast. When recurrence took place after mastectomy, all the patients who were menstruating or near menopause had undergone bilateral oophorectomy. In those well past the menopause, or in postoophrectomy cases, progression of disease was treated by an androgen, hypophysectomy, or cortisone. Fluoxymesterone was used as the androgen in these 23 patients, whose ages ranged from 35 to 63 years.

This new orally administered androgen was found to be effective in suppressing advanced mammary cancer in postmenopausal patients. Remission occurred in 7 (30%) of 23 patients—in 2, after hypophysectomy. Fluoxymesterone appears to be less masculinizing than injectable androgens in therapeutic doses. It can cause liver dysfunction, such as is seen with methyltestosterone.

Therapeutic Experience with Triamcinolone in Acute Viral Hepatitis. F. Orlandi, G. Marri, C. Manuali and others. Minerva med. 50:2182-2184 (July 4) 1959 (In Italian) [Turin, Italy].

The authors report on the effect of triamcinolone in 10 patients (9 women and 1 man) with acute viral hepatitis, who ranged in age from 19 to 44 years. On admission to the clinic, icterus had been present in each instance for a period of from 5 to 22 days. Triamcinolone was administered by mouth, and the initial daily dose was 3 mg. per kilogram of body weight. Eight patients received triamcinolone for 15 days; in these patients the daily dose of the drug was reduced to 12 mg. on the 8th day and to 4 mg. on the 11th day. The values of serum bilirubin declined and the levels of alkaline phosphatase became normal after 3 to 5 days of treatment. The values of serum transaminase also declined, while the serum lability tests became normal during the 2nd to 4th weeks of treatment. The histological examination of tissue obtained by puncture biopsies showed an improvement on the 4th to the 6th day of treatment. Triamcinolone in these first 8 patients gave results comparable to those obtained in the treatment of viral hepatitis with other steroids.

In the remaining 2 patients, the initial dose of triamcinolone was doubled on the 4th day of treatment and was kept high for the next 5 days but with no beneficial effect. Corticotropin (30 units per day given intramuscularly) was then substituted for triamcinolone on the 10th day in both instances. Laboratory tests became negative in one patient, and serum lability tests remained positive for 9 weeks. Corticotropin was withdrawn after 7 days of treatment in this first patient, but neither triamcinolone nor corticotropin had any effect in the second patient.

The authors believe that triamcinolone has a direct effect on the basic lesions of viral hepatitis and that, in case of no response, treatment with corticotropin or cortisone should be resorted to. Triamcinolone has the advantage over other steroids in that it can be used in lower doses and has no untoward side-effects.

A Clinical Study of the Effects of Hydrochlorothiazide on the Renal Excretion of Electrolytes and Free Water. W. Januszewicz, H. O. Heinemann, F. E. Demartini and J. H. Laragh. New England J. Med. 261:264-269 (Aug. 6) 1959 [Boston].

Hydrochlorothiazide, the 3,4,dihydro derivative of chlorothiazide in which the 3,4, double bond is saturated by 2 hydrogen atoms, was administered intravenously to a group of normal human subjects, and its effects on renal function were compared with the previously reported effects of chlorothiazide and of meralluride given under similar conditions. Dihydrochlorothiazide, like chlorothiazide, produced a marked increase in urine flow and total solute clearance, but the excretion of free water was not increased. Like chlorothiazide also, the dihydro derivative produced an increased excretion of sodium, chloride, and potassium. A chlorothiazide-similar reduction in glomerular-filtration rate was likewise produced by dihydrochlorothiazide, but in contrast to chlorothiazide it did not modify the clearance of uric acid in the dosage employed.

The findings obtained in this study support the hypothesis that dihydrochlorothiazide, like chlorothiazide, affects sodium and chloride reabsorption in both the proximal and the distal tubules, whereas meralluride acts only on the proximal tubule. They further tend to show that, although dihydrochlorothiazide is from 10 to 20 times as potent as chlorothiazide, it is qualitatively similar in its mode of action and its pharmacological effects. It may, therefore, be expected to be useful in the treatment of edematous states and hypertension under the conditions previously recommended for chlorothiazide.

Evaluation of Radioactive Iodine (I^{131}) as a Treatment of Hyperthyroidism. C. E. Cassidy and E. B. Astwood. New England J. Med. 261:53-58 (July 9) 1959 [Boston].

Radioiodine (I^{131}), although an effective form of treatment for hyperthyroidism, has the disadvantage that response of patients to a selected dose varies widely. A quantity that may restore normal thyroid function in one patient may prove entirely ineffective in another, and a similar dose may even induce lasting myxedema in a seemingly comparable case. To obtain a better understanding of individual variability in treatment, 200 patients with hyperthyroidism were observed from 1 to 7 years after treatment with I^{131}. Normal thyroid function returned in 85.5%, and permanent myxedema developed in 14.5%. Sixty-five per cent responded to one dose, and after 2 treatments 89% were cured of hyperthyroidism.

The method used by the authors to estimate dose did not yield better results than those obtained by other observers with one or another arbitrary method for selection of dose. Myxedema and multiple treatments were as frequent in women as in men. Patients having recurrent hyperthyroidism probably required a significantly larger number of treatments than previously untreated patients, but there was no significant difference in the occurrence of myxedema in the 2 groups. Complete or nearly complete disappearance of the goiter was found to be a reliable index of the effectiveness of therapy. The use of an antithyroid drug after I^{131} therapy did not diminish effectiveness as judged by the need for repeated doses, and yet in the patients who received both forms of treatment, myxedema developed significantly less often than in those who received I^{131} alone. The frequency of myxedema increases with time, since the complication developed in several patients more than 2½ years after treatment.

The Response of the Guillain-Barré Syndrome to Prednisone and ACTH. F. Di Nola and G. Giuliani. Minerva med. 50:2200-2201 (July 4) 1959 (In Italian) [Turin, Italy].

The case of a 55-year-old man with the Guillain-Barré syndrome, who was treated with prednisone and corticotropin (ACTH), is reported. About a week before admission to the hospital the patient had suffered from fever and diffused joint-muscle pain. This was followed a few days later by a lancinating pain in the lumbar region, which extended to the anterior part of the abdomen and was followed in a few hours by loss of motion in the lower limbs in which reflexes were no longer present. Poliomyelitis was suspected on admission. Because of the laboratory tests (serum tests were negative for influenza, types A and B, for adenovirus, and for poliomyelitis virus) and because the paralysis was symmetrical, the diagnosis of Guillain-Barré syndrome was made. Intestinal paralysis and spontaneous pneumothorax occurred on the 3rd and on the 6th day, respectively, after admission to the hospital. Prednisone was administered in a dose of 30 mg. per day for the first 3 days and of 20 mg. per day for the next 6 days; ACTH was given in a dose of 40 units per day during the following 5 days, and vitamins B_1 and B_{12} were also administered during this later period. The total dose of prednisone was 210 mg.; that of ACTH was 200 units. Gradual resolution of the symptoms was obtained. The pneumothorax disappeared 20 days after its onset, and the patient was able to walk about 40 days after admission to the hospital. On discharge, there was total functional recovery. The authors believe that the Guillain-Barré syndrome is neuroallergic in origin and attribute the clinical symptoms to an allergic-hyperergic reaction of the organism to the action of allergenic factors which may be either bacteria, viruses, or toxins.

The Treatment of Acute Barbituric Acid Intoxication: Clearing by Alkalization of the Plasma and the Urine. P. Mollaret, M. Rapin, J. J. Pocidale and J. F. Monsallier. Presse méd. 67:1435-1438 (July 25) 1959 (In French) [Paris].

The authors review the experimental studies they have carried out in dogs, and describe the methods of alkalization and the clinical results obtained in patients with acute barbiturate poisoning. Alkalization of the plasma hinders the penetration of phenobarbital into the cells, and increases the concentration of the toxic agent in the plasma. The increased urinary pH prevents tubular reabsorption of the barbiturates, and their renal elimination is markedly increased. Clinically, alkalization can be applied in 2 ways by giving perfusion of either isotonic or hypertonic sodium bicarbonate, but perfusion with this latter solution should be supplemented by artificial respiration and by an accurate control of arterial pH. While perfusions with isotonic sodium bicarbonate are easily performed and can be administered on a large scale, those with hypertonic sodium bicarbonate require intubation or a preliminary tracheotomy and, therefore, may be used only in specially equipped hospitals.

Of the 93 patients with barbiturate poisoning treated by the authors, 57 were subjected to alkalization of the plasma and the urine, and all recovered. This treatment substantially diminished the duration of coma. The plasma and urinary alkalization provoked by this treatment did not dispense from the necessity of the usual techniques of respiratory and circulatory reanimation, the importance of which in acute barbiturate poisoning has been emphasized by Danish authors.

Treatment of Acute Osteomyelitis. K. Stray. Tidsskr. norske laegefor. 79:831-834 (July 16) 1959 (in Norwegian) [Oslo].

From 1947 to 1958, 32 patients with acute osteomyelitis were hospitalized and treated. Large daily doses of penicillin were given, ranging, according to age, from 200,000 to 1,000,000 units or more. The effect was usually striking. The temperature, as a rule, became normal after about one week. The general symptoms disappeared, and the local symptoms rapidly regressed. Treatment with penicillin was continued beyond the time when the clinical symptoms had disappeared, usually for 3 weeks, sometimes longer. In 8 cases improvement did not occur until after operative intervention. In 27 patients the sedimentation reaction was normal before discharge, and in 5 it became normal shortly after discharge. Follow-up showed 31 patients to be clinically well; at long intervals one patient had suppuration from the affected bone of a few days' duration. On discharge the roentgen-ray picture was negative in 11 patients whose admission was an average of 5 days after the onset of the disease; in 13 patients admitted after an average of 15 days, changes in the bones were more or less visible; the 8 patients treated operatively were admitted after an average of 40 days from the onset. In acute osteomyelitis it is important to institute treatment with antibiotics as early as possible after the start of the disease and even when it is only suspected. With early and correctly applied treatment with antibiotics, close to 100% of the patients will recover clinically, and most of them will also become roentgenologically negative, provided that the disease is caused by microbes sensitive to the agent applied.

The Effect of Vaccine on Cancer Patients. J. B. Graham and R. M. Graham. Surg. Gynec. & Obst. 109:131-138 (Aug.) 1959 [Chicago].

The authors used Freund's adjuvant type of autogenous vaccines in 114 patients with advanced cancer of unfavorable prognosis. Most of the patients had gynecologic cancers. Thirteen died within the first month and are excluded from the analysis. The adjuvant devised by Freund is a combination of a light mineral oil, an emulsifying agent (arlacel A), and killed mycobacteria. It is mixed with equal parts of the antigen to produce a water-in-oil emulsion. With this adjuvant, the immune response to a standard antigen is greatly increased. Four forms of Freund's adjuvant were used.

The final step in the preparation of vaccine consisted of slowly adding the antigen to an equal volume of adjuvant while the mixture was repeatedly drawn into and expelled from a syringe to form a milky, water-in-oil emulsion. The volume of injected vaccine varied from 0.1 to 2.0 cc. and from 0.05 to 1.0 cc. in any site. The intramuscular (gluteal) route was used initially, but in 5 out of 25 patients cold abscesses developed. Subsequently, the intradermal (anterior thigh) route was used. Two sites were injected simultaneously. Fifty-six patients received vaccine only once; 45 received it on 2 or more occasions; and the maximum number of injections was 6 in 1 patient. The patients' clinical course was closely observed. All patients were treated prior to April 1, 1958, and have been observed for a minimum of 7 months. In 84% of the patients ulceration developed at the injection site that was tender and healed slowly over a period of from 3 to 4 months. In 2 patients of the 40 receiving cellular suspension, implants developed at the site of vaccination. Fifty-five of the 101 patients lived 7 months or more. Eight are living with demonstrable tumor, but it is quiescent and they are able to live in comfort. Fourteen are living and well with no demonstrable disease. The site of tumor does not seem to influence the result.

The patients who subsequently received irradiation therapy in the full dose (3,000 r or more, tumor dose) obtained better results than those receiving either palliative irradiation or chemotherapy. However, those receiving the larger doses of irradiation had a better prognosis before treatment was begun. No further treatment was given to 29 of these patients in whom gross tumor was present. Two of these have no demonstrable disease, and another is living with quiescent tumor. The best preparation of the antigen for vaccine appears to be the cellular suspension, for three-quarters of the patients receiving this lived 7 months or longer. Whole tumor homogenate, 1 M sodium chloride extract, and isotonic sodium chloride extract and suspension followed in that order of apparent effectiveness. The authors feel that autogenous vaccines with Freund's adjuvant can be given to cancer patients without serious sequels, and they gained the impression that some of the patients have been benefited.

Effect of Prolonged Use of Estrogens on Circulating Lipids in Patients with Idiopathic Hyperlipemia or Idiopathic Hypercholesteremia. E. B. Feldman, Chuni Wang and D. Adlersberg. Circulation 20: 234-242 (Aug.) 1959 [New York].

The low incidence of atherosclerosis in premenopausal women and the effects of gonadal extracts on serum lipids indicate the desirability of further clinical and biochemical studies. Ethinyl estradiol in minimal effective doses of 0.2 to 0.1 mg. daily in interrupted courses was administered to 7 men and 5 women with idiopathic hyperlipemia or idiopathic hypercholesteremia for an average period of 16 months. In the group with idiopathic hyperlipemia mean levels of total and esterified cholesterol, phospholipids, triglycerides, and total lipids fell 30 to 69% from pretreatment values. There was an increase in alpha-lipoprotein and a fall in beta-lipoprotein and the beta:alpha lipoprotein ratio. In the group with idiopathic hypercholesteremia mean levels of lipid fractions fell 11 to 39% from pretreatment values. Alpha-lipoprotein increased and beta-lipoprotein and the beta : alpha lipoprotein ratio decreased. A return toward pretreatment values within 2 to 5 months occurred in 5 patients placed on a placebo regimen.

Therapy was well tolerated. Side-effects included moderate gynecomastia, sensitive nipples, diminished libido, and uterine bleeding. Almost complete disappearance of extensive xanthomata tuberosa occurred in one man with idiopathic hyperlipemia after 14 months of therapy. The authors feel that the use of ethinyl estradiol provides a practical means of controlling abnormal serum lipid and lipoprotein levels.

Experience with Novocain (H3 Factor). P. Nebó. Hospital 56:157-160 (July) 1959 (In Portuguese) [Rio de Janeiro].

Eighty-six outpatients (54 men and 32 women), whose ages ranged from 30 to 87 years, and who were suffering from different diseases, were submitted to a treatment with intramuscular injections of a Novocain solution. The treatment was divided into 3 series of 30 daily injections, with an interval of 10 to 12 days between series. The proportion of Novocain was 2.5% in the first, and 2% in the second and third series. The pH of the solution varied between 3.5 and 4 in the first series and between 4 and 5 in the others. Preliminary laboratory tests were performed for each patient, as required by the individual circumstances. In addition, in each case a sensitivity test was given, consisting of a subcutaneous injection of 0.25 cc. of a 2% Novocain solution. In case of sensitivity to the drug, a desensitization treatment was given. This sensitivity test, as well as the laboratory examinations, was repeated before starting each new series of injections.

Thirty patients had completed the three-series treatment at the time this article was written. The diseases for which they were treated were hypertension in 10 cases, angina pectoris in 5, intermittent claudication in 4, osteoarthrosis in 4, hemiplegia in 3, and alopecia, diplopia, and duodenal ulcer in one case each. The results were evaluated in terms of general condition and specific improvements. The improvement in general condition was 100% in all patients, meaning better disposition, increased vitality, easy and tranquil sleep, greater muscular strength and mental power. As to the specific conditions, the improvement was termed optimal for 28 patients and good for the 2 suffering from diplopia and duodenal ulcer respectively. Besides these results, there was a definite rejuvenating effect of the Novocain therapy, represented by repigmentation and growth of the hair, softening and coloring of the skin, strengthening of the nails. Among the patients who had not yet completed their treatment (including one with prostatic disorder), there was improvement in several aspects.

PATHOLOGY

Exfoliative Cytology in Metastatic Cancer of the Lung. B. F. Rosenberg, H. J. Spjut and M. M. Gedney. New England J. Med. 261:226-231 (July 30) 1959 [Boston].

Of the patients with suspected metastatic tumors in the lung admitted to Barnes Hospital, St. Louis, in the years 1948-1958, 63 were found to have had cytological examinations of either sputum or bronchial washings or both. Thirteen cases were disregarded for lack of sufficient evidence of metastases. In the 50 patients suitable for study, a total of 122 cytological specimens were available. The clinical histories, the surgical or autopsy material, and the cytological smears were reviewed. The primary lesions were most often in the cervix and breast in the 31 women and in the pancreas and colon in the 19 men. In 45 of the 50 patients, the clinical diagnosis of metastatic lung cancer was confirmed histologically by one of the following methods: resections in 24, biopsies of the lung in 12, bronchoscopic biopsies in 5, autopsies in 2, and lymph-node biopsy or pleural fluid in 1 each. In the remaining 5 cases, a diagnosis was made on the basis of symptoms, x-ray findings, and presence of a known primary cancer. Four of these patients had positive cytological diagnoses as the only microscopic proof of cancer in the lung. The histories of these 4 patients are presented, and that of a 5th (not of this series) is reported to demonstrate the usefulness of accurate typing.

The cytological tests were positive in 19 (38%) of the 50 patients, and 5 others had suspicious smears. Although the percentage of positive results from exfoliative cytological studies was low, the authors regard it as encouraging. Furthermore, the typing of these lesions may have an important bearing on the clinical picture: correspondence of cytological type with that of the suspected primary lesion helps to confirm the diagnosis of metastatic disease. Discrepancy in type from a suspected primary source (as in the 5th case reported) may indicate that the pulmonary lesion is actually primary. The authors feel that these findings indicate a definite place for the cytological examination of sputum or bronchial washings in all patients with cancer who have pulmonary symptoms or an asymptomatic lesion in the chest on roentgenographic study.

Hepatic Involvement in Extrapulmonary Tuberculosis: Histologic and Functional Characteristics. R. J. Korn, W. F. Kellow, P. Heller and others. Am. J. Med. 27:60-71 (July) 1959 [New York].

Hepatic function was studied in 50 patients with extrapulmonary tuberculosis. Patients with pleural or pericardial effusion, but no other demonstrable extrapulmonary involvement, were excluded from this study. Abnormalities of hepatic function and of plasma proteins were found in all patients. The most frequent changes were impaired Bromsulphalein excretion and hyperglobulinemia. Analysis of these results revealed several patterns of hepatic dysfunction. These patterns were: (1) elevated serum alkaline phosphatase value and Bromsulphalein retention associated with space-occupying lesions (granulomas); (2) abnormal flocculation tests and hyperglobulinemia associated with certain chronic infections and inflammatory diseases; and (3) combinations of patterns 1 and 2 which may simulate intrinsic hepatic disease except for the relatively lower levels of serum bilirubin.

Liver biopsy specimens were obtained from 30 of the 50 patients. Granulomas were present in 24 of the specimens. Fourteen of 15 patients with elevated alkaline phosphatase levels had hepatic granulomas, as well as 10 of the remaining 15 patients who had normal alkaline phosphatase levels. In 16 of these 24 patients, the granulomas were easily recognizable, while in 8 patients only microgranulomas were seen. Focal Kupffer-cell hyperplasia and diffuse sinusoidal inflammatory reaction were sufficiently frequent to be characteristic of hepatic involvement in tuberculosis. Abnormality of the hepatic parenchymal cells was commonly observed, and in 3 patients free hyaline bodies were present.

Diabetic Glomerulosclerosis: Electron and Light Microscopic Studies. M. G. Farquhar, J. Hopper Jr. and H. D. Moon. Am. J. Path. 35:721-753 (July-Aug.) 1959 [Ann Arbor, Mich.].

Diabetic glomerulosclerosis is a frequent complication of diabetes mellitus of long duration, despite the efficacy of insulin therapy. Although the glomerular lesions have been studied extensively, the pathogenesis of this condition remains obscure. The present investigation was conducted in order to obtain further information on the evolution of diabetic glomerulosclerosis through the combined use of electron and light microscopic techniques in renal biopsies of diabetic patients. Renal biopsy specimens from 7 patients were studied. The severity of renal impairment varied greatly, ranging from 3 patients with normal renal function and blood pressure to 2 patients with the classical features of the Kimmelstiel-Wilson syndrome (massive proteinuria, retinitis, hypertension, edema, azotemia, and hypoalbuminemia). On examination by light microscopy, diabetic glomerulosclerosis was characterized by gradual obliteration of glomeruli by the deposition of hyalin. Hyaline deposit was evident initially near the afferent arteriole and subsequently extended radially to involve more peripheral loops.

By electron microscopy, thickening of the basement membrane proper was one of the earliest manifestations of diabetic glomerulosclerosis; some degree of thickening, up to 10 times normal, was observed in all glomeruli. The earlier lesions, i. e., the smaller deposits of hyalin, were similar in appearance to the basement membrane and were frequently continuous with it. Their presence between the cell membranes of adjacent endothelial cells (interendothelial) suggested that they represented an extracellular product of the glomerular endothelium. With greater accumulation of hyalin, islands of endothelial cytoplasm appeared isolated by the expanding masses. Finally, the capillary lumen was obliterated. In the later stages, hyalin showed altered staining characteristics and was more heterogeneous in texture by electron microscopy. The nodular lesions developed from the diffuse lesions by enlargement of the hyaline deposits, as originally suggested by Bell. Fibrinoid deposits or "exudative lesions" of glomeruli were present in 2 patients with the most advanced glomerular alterations. This substance could be distinguished in electron micrograms by its great density. It was subendothelial in position, lying between the endothelial cell membrane and the basement membrane. The epithelium was not altered early in the course of hyaline deposition. Later, however, some loss of the epithelial foot processes was seen in severely damaged glomeruli. The fine structural alterations of glomeruli in diabetes mellitus could be differentiated from those occurring in disseminated lupus erythematosus, nephrosis, amyloidosis, and preeclampsia and eclampsia.

Aging and Osteoarthritis of the Human Sternoclavicular Joint. M. Silberberg, E. L. Frank, S. R. Jarrett and R. Silberberg. Am. J. Path. 35:851-865 (July-Aug.) 1959 [Ann Arbor, Mich.].

The aim of the investigations described was to analyze the role of articular aging in the pathogenesis of osteoarthritis. Sternoclavicular joints of 200 individuals, ranging in age from the 1st to the 10th decades, were studied for the existence of age alterations and osteoarthritis, with particular reference to the role of early growth processes. Joint lesions of both types appeared during the third decade. The incidence and severity of osteoarthritis increased up to the age of 80 years. In individuals over 90 years of age, the incidence of severe arthritis was strikingly decreased. The lesions found in males were more severe than in females, and Negroes seemed to be more susceptible than whites. There was a positive correlation between osteoarthritis and diabetes and chronic renal disease, and between severe osteoarthritis and obesity; however, no such correlation was found to exist between osteoarthritis and arteriosclerosis. The coexistence of atherosclerosis and osteoarthritis appears to be merely coincidental. The relationship between arthritis and obesity does not seem to be based on mechanical factors. The occurrence of severe osteoarthritis in comparatively young individuals with diabetes is under investigation. The possible significance of chronic renal disease in the development of osteoarthritis likewise requires exploration. In both of these conditions hormonal imbalances exist, which may possibly act as mediators in the development of severe joint disease, since hormones exert profound influences on articular cartilage.

Hyperplasia and hypertrophy of the articular cartilage cells occurred early in the aging process and were associated with changes in metachromasia and loss of PAS-positive (periodic acid-schiff) staining in the matrix. These biochemical and biophysical changes in the intercellular substance are thought to interfere with the restraining influence usually exerted by the matrix on cell growth. As a consequence, the dormant growth potential of the cartilage cells may be released, and the ensuing growth may set off the chain of events which lead to the complex structural lesion of osteoarthritis.

Studies on the Pathology of Low Back Pain. C. Hirsch. J. Bone & Joint Surg. 41B:237-243 (May) 1959 [London].

Five hundred autopsy specimens of the spinal column from persons of all ages were collected, and the intervertebral disks of the lumbar spine were examined for their anatomic appearance. Gross and microscopic examination showed that disk degeneration starts as an avascular necrosis. In the lower disks fissures and ruptures occur early, beginning mostly at the border between the nucleus and the cartilaginous plates and extending toward the center of the nucleus. The nucleus is becoming more compact, with diminished stainability, the collagenous structure being visible. These dry necrotic areas can often be seen as early as the third decade. When ruptures in the annular fibers occurred close to the outer border of the disk, a connective tissue reaction occurred in the area of the annulus. Vessels grew in from the long ligaments, and in the lower lumbar disks from the posterior ligament. These foreign elements appeared as vascular granulation tissue. It was found that in the lower lumbar disks the ingrowth of vessels into the posterior part of the disk was common between the ages of 30 and 50 years, that is, when low back pain shows the highest incidence.

These findings suggested that avascular necrosis followed by mechanical stress was the main cause of early degenerative changes in the lower lumbar area. In an attempt to find out how this would produce pain, a series of disk puncture experiments were made. A lumbar puncture needle was introduced transdurally into the posterior area of a lumbar disk under roentgenographic control. Isotonic sodium chloride solution was injected. In some disks less than 1 cc. could be instilled even with strong pressure on the syringe. In these cases the patient felt no pain. In other disks more than 1 cc. could be injected easily, and pain occurred when the pressure was raised. In these cases the patient stated that it was the same pain that he usually had when his backache was present. When the pressure was released, the pain disappeared immediately if very little procaine was injected. These findings suggested that the pressure inside the disk had produced stress on the posterior area of the annulus and caused a deformation which affected the posterior ligament with its sensitive nerve elements. The conclusions drawn from the anatomic findings and from the disk puncture experiments are as follows: 1. Disk degeneration starts as an avascular necrosis. 2. In the lower lumbar area the disks deteriorate early because of mechanical stresses. 3. During certain early periods of degenerative changes a mechanical disorder between the annulus and the posterior longitudinal ligament may cause tiredness and pain. 4. When the disk is completely degenerated and has lost its physical properties, backache disappears.

PUBLIC HEALTH

The Importance of ECHO Virus in the Etiology of Poliomyelitis-Like Diseases. U. Krech. Schweiz. med. Wchnschr. 89:676-680 (June 27) 1959 (In German) [Basel, Switzerland].

Numerous infections due to enteric cytopathogenic human orphan (ECHO) virus, type 9, were reported in Switzerland between 1956 and 1958. The epidemiologic pattern of these infections was in many respects similar to that of poliomyelitis; they may be either clinically latent or characterized by fever, exanthem, and meningitis. Because the clinical course of diseases caused by ECHO virus, type 9, may vary from one epidemic to another, a correct diagnosis can be made only by means of virologic examination. ECHO virus, type 4, was also isolated in patients with aseptic meningitis in 1956. Among members of the ECHO virus group, types 5, 6, 14, and 21 may be responsible for poliomyelitis-like diseases. The etiological significance of the other types has not yet been sufficiently elucidated.

The Epidemiology of Poliomyelitis in Switzerland in 1958. M. Schär. Schweiz. med. Wchnschr. 89:699-701 (June 27) 1959 (In German) [Basel, Switzerland].

In 1958 only 176 cases of poliomyelitis were reported in Switzerland; 101 of these were paralytic, and 76 were nonparalytic. Serologic and virologic examinations revealed that in the 76 (65%) nonparalytic cases the disease was not caused by poliomyelitis virus, but mostly by enteric cytopathogenic human orphan (ECHO) virus. In Italy and in Austria during that year poliomyelitis epidemics were characterized by a high mortality rate, while in France and in Germany the disease was rather mild. Only 15% of the paralyzed patients in Switzerland under the age of 20 years had received poliomyelitis vaccine 2 or 3 times, whereas 45% of the patients who were not paralyzed and more than 60% of the healthy population belonging to the same age group had previously been vaccinated. In 1956 the highest percentage of paralytic cases was found in children ranging in age from 3 to 11 years. In 1958, however, the morbidity was highest among infants, children up to the age of 3 years, and adults. This change in the age distribution of paralytic cases may be attributed to the mass-vaccination of school children with Salk vaccine.

BOOK REVIEWS

Radiation Therapy. By Walter T. Murphy, M.D., Director of Therapeutic Radiology, Roswell Park Memorial Institute, Buffalo, N. Y. Cloth. $25. Pp. 1041, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

This well-written book has an author index and a subject index. The illustrations are numerous and excellent. The various chapters are well organized and complete, each covering a particular disease site or type. Anatomy, clinicopathological aspects, methods of treatment, and prognosis are included. Methods and opinions other than those of the author are given in detail. A comprehensive list of references, which in themselves should prove of great value to the student, is found at the end of each chapter. The chapter on physics is brief and to the point. The omission of a rehash of the various books available devoted entirely to this subject is appreciated. This is a monumental piece of work. It should be part of the library of every physician who treats patients with cancer and for all who practice radiotherapy.

Cancer in Families: A Study of the Relatives of 200 Breast Cancer Probands. By Douglas P. Murphy, M.D., and Helen Abbey, Sc.D., Assistant Professor of Biostatistics, School of Hygiene and Public Health, Johns Hopkins University, Baltimore. Cloth. $2.50. Pp. 76. Published for Commonwealth Fund by Harvard University Press, Cambridge 38, Mass.; Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, England, 1959.

The purpose of this book was to see whether cancer occurred more frequently in the relatives of persons who had cancer than in the relatives of persons who did not and, if so, whether the difference was greater in some relationships than in others. An introductory section reviews previous research on the subject and draws valuable lessons as to methodology from the conflicting and inconclusive publications of the past. Section 2 describes the authors' methods and shows to what lengths the authors went to secure comparable groups of probands with and without cancer. The findings are summarized in 47 pages of tables and text in section 3 and lead (page 64) to the conclusion (section 4) that, if a familial tendency to develop cancer did exist, it was not strong enough to be detected in this sample of 200 breast cancer patients. A critical comparison with a previous study by Jacobsen is made in appendix A. Appendix B gives data obtained from additional female relatives discovered in a resurvey and reaffirms the conclusion that no familial tendency was discernible in this study.

The authors deserve commendation for the painstaking exposition of the statistical methods they used in their effort to avoid criticisms leveled at previous work. Their conclusion is important to everyone concerned with the cancer problem, and their methods deserve the close attention of other investigators working at research in this field.

Symposium on Nuclear Sex. Edited for Organizing Committee by Secretary, D. Robertson Smith, M.A., M.D., and William M. Davidson, M.D. Foreword by Professor Robert Platt, M.D. Cloth. $3.50. Pp. 188, with illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; William Heinemann, Ltd., 99 Great Russell St., London W. C. 1, England, 1958.

This small volume consists of a series of papers presented in 1957 at Kings College Hospital Medical School in London. A brief historical introduction by Dr. Murray L. Barr describes the circumstances that led, some eight years earlier, to his recognition of sexual dimorphism in the nuclei of mammalian cells. The first seven papers are devoted to the morphology and the genetic significance of the so-called sex chromatin, and the remaining papers deal with applications of "nuclear sexing methods" in clinical medicine and include discussions of sex chromatin in congenital errors in sex development, in teratomas, and in tumors. Each paper is accompanied by a bibliography and a discussion, and there are numerous illustrations throughout the text, including many well-reproduced photomicrographs. This book can be recommended as a stimulating introduction to this fascinating and rapidly developing field.

Diagnostic Biochemistry: Quantitative Distributions of Body Constituents and Their Physiological Interpretation. By Halvor N. Christensen, Ph.D., Professor of Biological Chemistry and Chairman of Department, University of Michigan, Ann Arbor. Cloth. $6.50. Pp. 291, with illustrations. Oxford University Press, Inc., 417 Fifth Ave., New York 16, 1959.

This volume was prepared to be used as a textbook for advanced students, as a supplement in a beginning course, or to refresh the physician's understanding of biochemistry. Half the book is devoted to acid-base balance and a thorough presentation of anion and cation distribution and balance and their relationship to acid-base balance. The rest is concerned with the distribution and transport of nitrogen compounds, proteins, lipids, carbohydrates, iodine and thyroid hormones, steroids, and heme precursors and products. An outstanding feature of the book is the inclusion of a series of problems at the end of each chapter. Many of these are practical biochemical problems and have been taken from case reports.

QUESTIONS AND ANSWERS

RECORDING OF POLIOMYELITIS IMMUNIZATION

To the Editor:—*Many boys admitted to our school have had one or more injections of poliomyelitis vaccine, but we are frequently unable to determine the exact number of injections or when they were given. What plan of poliomyelitis immunization procedure should be followed when records are not available? Each boy is given a card showing his immunization record when he is released. Is there any practical method of having this information available on a national basis?*

Earl N. Saunders, M.D., Marianna, Fla.

Answer.—When no record of the past poliomyelitis vaccine injections is available for school children, and the parents cannot furnish a signed note concerning them, the recommended series should be given. The usual precautions and contraindications for immunizing biologicals should be observed. The interval between injections can be as long as one year without impairing the response. Booster injections are recommended. Most school systems are attempting to keep a complete medical record, including the inoculations of each child prior to and after his entrance to the kindergarten or first grade. This record, together with his medical record through school, will become a part of his permanent school record and is transferable when he enters another school. This may be the best solution to the problem of dependable records of immunizations on a national basis. The National Congress of Parents and Teachers, 700 N. Rush St., Chicago 11, has made this a part of its program of continuous health supervision of all children from birth through their school experience. Samples of the instructions the congress furnishes its local and state chapters may be obtained from it.

CIRCUMSCRIBED CORTICAL ATROPHY

To the Editor:—*What is the treatment for a patient with circumscribed cortical atrophy (Pick's disease)? Is electroshock therapy or administration of glutamic acid in high doses of any value?*

M.D., New Jersey.

Answer.—This is a degenerative disease of the brain, characterized by focal atrophy of cortical cells chiefly in the frontal and temporal regions. It produces mental changes of progressive dementia, emotional dulness, confabulation, and delusions, and the prognosis is unfavorable; there is no special treatment. Electroshock treatment is contraindicated, since it would increase the confusion. If the patient becomes agitated, difficult to manage, profoundly depressed, or suicidal, however, a few electroshock treatments might alleviate these complications. Administration of glutamic acid may be tried, as may chlorpromazine, but the former has not proved to be of value and the latter is only for symptomatic relief.

Answer.—There is no known treatment of this disorder except to relieve the patient of symptoms as they arise. If the patient is disturbed, he may be helped by administration of tranquilizing drugs and proper environmental control. When he is severely depressed, stimulating drugs should be given. There are feeding and communication problems, because of the aphasia and the apraxias which develop, and the nursing personnel must have some understanding of the disease. Electroshock treatment and administration of glutamic acid are of no value.

SYMPTOMS OF PARESTHESIA

To the Editor:—*A 36-year-old woman, while sightseeing in a cave last summer, was suddenly unable to straighten her back and had chills for three days. One month after this she had a sensation in the legs which was felt more in the left than in the right and was described as "like the crawling of ants." She was referred to a neurologist and after a thorough examination was told that there was no organic illness. She was given a series of vitamin injections. The sensation in the legs disappeared two months after the series was completed, but two months ago the sensation recurred in her arms. A detailed history, a complete physical examination, and the usual preliminary laboratory tests have not indicated any disease entity. What is the diagnosis?*

M.D., South Dakota.

Answer.—This is likely to be multiple sclerosis, because the sudden onset, remission, and the recurrence in a different region are quite characteristic. Multiple sclerosis is about the most common organic nervous disease in the northern part of the United States. The symptoms of the first two or three attacks usually disappear completely, but later relapses bring increasing disability. There is no specific treatment, but five blood transfusions (500 cc. given every five days) may help in the acute relapses. Prolonged bed rest is desirable, if

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

feasible, and the patient and her family should move to a warmer climate. The average duration of multiple sclerosis is 27 years.

Answer.—A definite diagnosis cannot be made from the information available. The possibilities for differential diagnosis would be a protruded intervertebral disk ("slipped disk"), multiple sclerosis, multiple sensory neuritis, and an emotional disturbance. If the cerebrospinal fluid studies give normal results, a reexamination of the nervous system should be made in 6 to 12 months. The possibility of emotional conflict deserves detailed inquiry to obtain background data and an account of circumstances surrounding the onset of complaints. Phobic reactions are often associated with episodes of hyperventilation, muscle hypertonus, "chilly" sensations, paresthesia, palpitation, vertigo, and a premonition of imminent loss of consciousness. A diagnosis of an emotional disturbance should be substantiated by psychological evidence.

PENICILLIN ANAPHYLACTIC SHOCK

To the Editor:—*A 6-month-old infant whose growth and development had been normal developed otitis media secondary to a mild chronic upper respiratory infection. The boy was given an injection of a standard antibiotic combination of procaine penicillin G, streptomycin, and dihydrostreptomycin. A few seconds after the injection had been given the child had all of the signs and symptoms compatible with anaphylactic shock. Mouth-to-mouth artificial respiration and other care restored spontaneous breathing in about 30 minutes, and with this there were some clonic convulsive movements of the lower extremities and the mandible. The infant was restless and dazed for the next 30 minutes and then slept for two hours. His breathing was normal during the rest and he was normal in every respect when he awakened. His growth and development in the two months since has been normal. What was this reaction and what should be the future management of injections, immunizations, and administration of antibiotics?*

Berryman Green, M.D., Laguna Beach, Calif.

Answer.—The most likely diagnosis would be severe anaphylactic reaction, and the offending allergen was probably the penicillin. A reaction of this severity is rarely due to procaine or streptomycin. Inadvertent intravenous injection, which would have contributed to the rapid onset of the reaction, may have occurred. The prolonged apnea after the injection is unusual. The streptomycin may have exerted some degree of neuromuscular blockade, causing paralysis of the respiratory muscles (Brazil and Pinto Corrado: Curariform Action of Streptomycin, *J. Pharmacol. & Exper. Therap.* **120**:452 [Aug.] 1957). The convulsive movements were probably a result of the cerebral anoxia during the period of prolonged apnea. This child should never be given penicillin parenterally in the future and its administration should be avoided completely, if possible, since reactions can occur from tablets and sprays taken orally or nasally. If antibiotic therapy is necessary administration of the medicament should be by mouth. Before immunization of any type skin and eye sensitivity tests must be done. Influenza and poliomyelitis vaccines should be carefully selected, since some of these preparations contain traces of penicillin. A recent paper by Zussman (*Am. Pract. & Digest Treat.* **10**:786-788 [May] 1959) contains more information.

SIDE-EFFECTS OF GRISEOFULVIN

To the Editor:—*Does the new antibiotic griseofulvin have any undesirable or harmful side-effects?*

Bruno L. Griesman, M.D., New York City.

Answer.—The usual therapeutic doses of 1 or 2 Gm. per day for adults and about 25 mg. per kilogram of body weight for children of griseofulvin have not, as yet, caused an acute toxic reaction. There have been a few reports of drug eruptions, mild and evanescent occipital headaches, and evanescent depression of the polymorphonuclear leukocytes in children. As with any new drug, it is essential to have the patients receiving griseofulvin under regular observation and to do repeated examinations, including blood cell counts. There can be no certainty as to the possible occurrence of unusual reactions in a hypersensitive patient, nor can anything be predicted about the possible effects which may appear years after the administration of the drug. The record of griseofulvin indicates that it is an orally effective agent against superficial fungous infections of the skin, hair, and nails (with the exception of infections by Candida albicans) and that it has a remarkably low toxicity, if any.

THYROID MEDICATION IN PREGNANCY

To the Editor:—*Several years ago the diagnosis of hypothyroidism was made clinically on a patient, without laboratory confirmation by either basal metabolism or protein-bound iodine test findings. The patient is now three months pregnant and has no signs or symptoms of hypothyroidism, but she continues to take 120 mg. of thyroid extract daily. Should she continue the thyroid therapy for the rest of this pregnancy or can it be discontinued?*

Sheldon M. Biback, M.D., Seattle, Wash.

Answer.—This patient should continue taking the thyroid extract during pregnancy, at the same dosage that she was taking prior to pregnancy. If she has been euthyroid on this dose, it is possible that she may have achieved sufficient inhibition of the thyroid gland to cause hypothyroidism if the medication were to be discontinued at this time. Her thyroid status should be evaluated after her pregnancy.

PHYSIOLOGICAL JAUNDICE IN THE NEWBORN INFANT

To the Editor:—*How soon after birth does the serum bilirubin content reach its maximum level, and what are the highest levels recorded in evaluations of physiological jaundice of the newborn infant? Should an infant have an exchange transfusion when the serum bilirubin level reaches 20 mg. per 100 cc., even if there is no evidence of hemolytic disease?*

Henry Krochmal, M.D., Meriden, Conn.

Answer.—In the term baby the peak level of the blood serum bilirubin is reached in four days. In the premature infant it is reached somewhat later, usually in seven days. In the normal newborn infant the level of serum bilirubin should not exceed 15 mg. per 100 ml., but Davidson and co-workers (*Am. J. Dis. Child.* 61:958 [May] 1941) found that of 106 consecutive normal newborn infants 2 had a serum bilirubin level exceeding 20 mg. per 100 ml. In the premature infant, as Kock and co-workers (J. Pediat. 55:23 [July] 1959) have shown, 4 of 100 premature infants had levels between 30 and 40 mg. per 100 ml. Three of these developed symptoms and signs of kernicterus. While this may be called physiological jaundice, it must be realized that an increase could be influenced by the administration of certain sulfonamides and high doses of water-soluble synthetic vitamin K.

Irrespective of the cause of the hyperbilirubinemia it is advisable to keep the level of serum bilirubin below 20 mg. per 100 ml. during the first 5 days of life in term infants and for a longer time in premature infants. The level can be anticipated to be higher than normal if the bilirubin level exceeds 4 mg. per 100 ml. at birth or is greater than 10 mg. in the first 24 hours of life, 14 mg. in the second 24 hours, or 17 mg. at any time in the 2nd to 4th days of life. A serum bilirubin level higher than normal is an indication for replacement transfusion, regardless of the cause.

HEART DISEASE AND DRIVING

To the Editor:—*Please clarify the matter of employment for patients after myocardial infarction. Would it be advisable to return a patient previously employed as a trailer truck driver to this position after his recovery from coronary occlusion? Does the physician share the responsibility of public liability in the event of an accident occurring after another occlusion while driving?*

M.D., Minnesota.

Answer.—Patients who have complete recovery from myocardial infarction, with the absence of chronic cardiac decompensation and anginal pain that is difficult to control, are employable. The ideal type of work is sedentary, including light manufacturing, or, in general, occupations that do not entail prolonged periods of strain or maximum physical exertion. Truck driving or the driving of any common carrier by these patients is contrary to the public interest and safety, even though the patient may be able to do so without symptoms. The public hazard in the event of another attack while driving is obvious. I believe the physician has a moral obligation to do everything in his power to dissuade such patients from this type of employment. I also believe that the employers of such patients should be informed of the public hazard incident to continuance of the employment.

Answer.—A physician may be held liable for the damages which result from his negligence. If the patient whom the doctor has treated for a coronary occlusion should not engage in his regular employment because of the physical requirements of the job, it would seem that there is at least a medical and a moral obligation to so inform his patient. There may even be a legal liability.

PARAPLEGIA AND PAIN

To the Editor:—*A 45-year-old man has been a paraplegic for about two years. He has made a fair adjustment to this difficulty, but progress has been limited because of pain. He complains of an aching pain in the pelvis and lower middle part of the abdomen. It occurs with activity and increases with sitting and when riding in a car. The pain becomes severe after the patient has been up one or two hours and forces him to lie down. He is not always consistent in location or description of the pain. He has an indwelling Foley catheter, his bowel function is irregular, and he feels the pain is worse with full bowel or bladder. A neurosurgical consultant suggested division of the spinal cord, but the patient opposed this procedure. Analgesics give him some relief from the pain, but he does not want to take hypnotic drugs regularly. He has some phantom-like pains, but these do not distress him very much.*

Ralph V. Harr, M.D., Santa Rosa, Calif.

Answer.—The following features suggest a major psychogenic component in the pain of this patient: (1) any activity makes the pain worse; (2) he has difficulty in describing and localizing the pain; and (3) he has phantom pains. Psychiatric evaluation of this patient is indicated. Recommendations for or against psychotherapy, including hypnosis, should be made, and the psychiatrist ought to determine whether the patient would be willing to accept management as outlined. Assuming that the patient does not have any other disease (such as malignancy) and the paraplegia is complete, a preliminary lumbar puncture and the injection of saline solution, along with much positive suggestion, should be done. This placebo type of procedure may reveal evidence concerning the patient's suggestibility. A step-by-step ascending spinal anesthetic should be administered to the sensory level above the initial cord injury; if pain is completely relieved then operative management can be considered further. The possibilities include cordotomy in the cervical or upper thoracic region, complete transverse myelotomy in the lower thoracic region of the cord (perhaps combined with a separate excision of the conus medullaris to improve bladder function), or alcoholic injection of the cauda equina. The actual decision would depend on the tonus of the muscles of the limbs and the function of the bladder, as measured by cystometric studies both before and during the administration of the spinal anesthetic.

PROBABILITY OF FETAL ANOMALIES

To the Editor:—*A couple's first child was stillborn. The fetal development was apparently normal, and delivery was not premature. Death was attributed to an umbilical clot. Their second child is normal, but the third child has a cleft palate. There is no family history of cleft palate, but two cousins of the parents have septal heart defects. What advice should the parents be given before another pregnancy is started?*

William J. Kibler, M.D., Tonawanda, N. Y.

Answer.—The umbilical clot is not a complete explanation of the death of the first child. If the cause of death is considered as unknown, a slightly increased risk of a stillbirth is a probability in subsequent pregnancies, although specific statistics cannot be supplied. The probable recurrence of cleft palate in future children is increased by 2 or 3% over the probability of its occurring in a family for the first time. Risks of this degree scarcely constitute a contraindication to future childbearing. Should there be another stillbirth there would be psychic trauma, but this usually is not a lasting problem. In case of cleft palate correction by operative procedures may be anticipated. The facts as they are currently understood should be presented to the family and they should then make the decision concerning further children.

MIGRAINE AND HYPNOSIS

To the Editor:—*A 40-year-old woman has severe migraine and receives only moderate relief from the usual treatment. Would hypnosis be effective? Would it have to be repeated in anticipation (or for relief) of each attack?*

Calvin P. Wallis, M.D., Ocean City, N. J.

Answer.—Migraine often yields to hypnosis when other types of therapy have been inadequate. The benefit is sometimes temporary but usually of long duration. Hypnosis, by itself, is not therapeutic, nor can much be expected from direct posthypnotic suggestion. Effective therapy lies in use of the hypnotic state for (1) reeducation of the patient in relation to her symptom-complex and (2) corrective suggestions for her personality problems. The problem is best managed by a psychiatrist or by a general practitioner who has experience with the use of hypnosis.

BACTERIOPHAGE

To the Editor:—*What is the status of the use of specific bacteriophage as a therapeutic agent in the treatment of staphylococcic infections?*

W. B. Bissell, M.D., Patchogue, N. Y.

Answer.—Bacteriophage offers little promise as a therapeutic agent for the treatment of staphylococcic infections. It is necessary in each case to use the strain of bacteriophage specific for the type causing the infection. To date 29 different bacteriophage types have been recognized, and these account for no more than 67% of reported staphylococcic infections. When the offending organism has been isolated in pure culture and typed by bacteriophage, substantial quantities of the specific bacteria-free bacteriophage required for therapy must be obtained or produced. Therapeutic bacteriophage is not generally available as a commercial product.

If past experience with the bacteriophage therapy of shigellosis is a valid example, it must be expected that staphylococci will often become resistant to bacteriophage. When this occurs, continued administration of bacteriophage is useless. The risk of side-reactions is likely, because bacteriophage preparations are filtrates of bacterial cultures of staphylococci and consequently contain soluble products of bacterial origin which may be toxic.

INTERMITTENT CLAUDICATION

To the Editor:—*How much disability does intermittent claudication usually cause? To what extent would a doctor doing office work be disabled? After walking two or three blocks my legs ache and I have to rest or slow down.*

M.D., Illinois.

Answer.—Intermittent claudication seldom limits walking distance to less than one-half block, if the patient walks slowly. It rarely interferes with the office work a physician performs, even though he is on his feet most of the time. It takes sustained walking to induce the discomfort. Careful studies have shown that intermittent claudication does not often become a progressive disability. It is an interesting observation that, in a patient suspected of having intermittent claudication, the physician is not usually able to elicit this symptom by having the patient walk within the confines of his office.

DECREASING BLOOD CHOLESTEROL LEVEL

To the Editor:—*A 53-year-old woman with moderate hypertension which is fairly well controlled with Rauwolfia medication has a blood cholesterol level of around 400 mg. per 100 cc. After several months on a low-fat diet, and the use of corn oil in cooking, a test of the patient's blood cholesterol level showed a slightly higher figure. She is overweight and has not succeeded in reducing. She is concerned about the cholesterol values. How serious is this? What other measures can be taken, and how effective are the newer drugs for the reduction of cholesterol levels?*

M.D., Kansas.

Answer.—Many authorities believe that elevated blood lipid levels are related to atherosclerotic heart disease and recommend measures to lower the blood lipid levels when they are elevated. Studies should first be done to rule out possible underlying disorders associated with elevated lipid levels such as diabetes mellitus and hypothyroidism. Control of these diseases would help to reduce lipid levels. The cholesterol level can be lowered by placing this patient on a reducing diet including only 40 to 50 Gm. of fat, with the addition of 30 cc. of corn oil administered three times daily. The latter can be used in cooking or taken as an appetizer blended with tomato juice and egg white. Should the above program fail, nicotinic acid in doses of 1 Gm. three times a day can be tried, for it has been shown to cause lowering of lipid levels. The side-effects, flushing, mild urticaria, and nausea, are usually transient and disappear after three or four days. Periodic examinations of blood sugar level and liver function are advisable, if the latter therapy is used, in view of reports of elevation in blood sugar levels in patients taking the drug as well as possible occasional hepatic dysfunction.

PRESCRIPTION OF NARCOTICS

To the Editor:—*What amounts of narcotic preparations could one safely give orally to a patient over a period of several months and not cause addiction? With some illnesses such as arthritis, frequent headaches, or intervertebral disk trouble pain may be annoying or unbearable. Could a patient be given a prescription for tablets to take orally when needed for sleep?*

Walter R. McLawhorn Jr., M.D.,
Fountain Inn, S. C.

Answer.—The possibility of addiction of a patient as a result of administering narcotics in the treatment of chronic diseases is the same, regardless of whether the drugs are for oral or parenteral use. The hazard is in proportion to the extent to which the patient is permitted to regulate his own dosage schedule. The first thought should be whether or not the condition warrants the risk involved in making a supply of narcotics available to the patient. Except for short-term treatment of a patient with severe acute exacerbations of "arthritis, frequent headaches, or intervertebral disk trouble" the use of narcotics would generally be unwise. If the etiological factors involved cannot be eliminated, and the patient fails to respond to nonnarcotic palliative therapy with salicylates, adrenocorticosteroids, physical therapy techniques, or surgery, the physician may be justified in prescribing a few orally administered doses of narcotics, trying first the less potent analgesics, such as d-propoxyphene or codeine alone or in combination with acetylsalicylic acid. If such drugs fail, a few doses of the more potent orally effective narcotic analgesics, such as 2 or 3 mg. of levorphan or 50 to 100 mg. of meperidine, may be prescribed. Whenever more than this is needed the patient should be admitted to a hospital, where adequate amounts of narcotics may be given parenterally under the close supervision of the physician, for as brief a period as possible.

RECONSTRUCTION OF FALLOPIAN TUBE

To the Editor:—*A 19-year-old woman had a bilateral salpingectomy and unilateral ovariectomy performed two and one-half years ago because of tuberculous salpingo-oophoritis. She also received antituberculosis therapy for 18 months. She now is asymptomatic and wants to have children. Can salpingoplasty be done in this situation, and what would the prognosis be?*

M.D., Virginia.

Answer.—Whether or not an operation is indicated in this case depends on a thorough investigation. First one must be sure that the husband is fertile. A hysterogram will define the uterine cavity and the cornual portion of the tubes and any portion of a tube that might remain. A curettage should be done to rule out tuberculosis of the endometrium. The type of operation needed will depend on the findings. If no portion of a tube that can be used for a tubal plastic procedure remains, then the Estes operation could be done. In this the ovary is implanted in the uterine wall, with a portion of the cortex in the uterine cavity, so that ovulation occurs in the cavity and the ovum is deposited on the endometrium.

The Estes operation is successful in about 6% of patients, and the one remaining ovary might be damaged by the operation, with a loss of its function. This loss for a 19-year old-girl would be unfortunate. I cannot give an opinion as to the reactivation of the tuberculous process. My advice would be adoption of children, unless enough tubal tissue remains to allow a good prognosis with plastic repair.

PERSPIRATION AND EMOTIONS

To the Editor:—*A 17-year-old girl has excessive axillary perspiration. The usual deodorants or anticholinergic drugs have not been effective. I would appreciate suggestions that would assist the treatment of this patient.*

James A. Freeman Jr., M.D.
Dawson Springs, Ky.

Answer.—Hyperhidrosis may be due to thermal, physical, metabolic, neurogenic, and psychogenic factors. When excessive axillary sweating does not respond to chemotherapy, one ought to consider the possibility that psychogenic factors may be involved. An increase in perspiration from the skin of the axillae, palms of the hands, and soles of the feet due to emotional stress, pain, fear, and excitement is common. Kuno and co-workers found that concentration on mental arithmetic problems induced axillary sweating in youngsters 9 years of age or older. Shelly and Hardy demonstrated that apocrine glandular function is stimulated by emotional stress.

The following signs can be used to differentiate between thermogenic and psychogenic hyperhidrosis: 1. Deliberate exposure to elevated and environmental temperatures does not cause an increase in emotional sweating. 2. Thermogenic hyperhidrosis has a greater tendency to produce skin lesions than does the emotional form. 3. According to Kosuge, emotional hyperhidrosis decreases or subsides during sleep, whereas thermal sweating usually increases during sleep. If emotional stress is found to be the cause, psychotherapy should be helpful.

BEE VENOM AND ARTHRITIS

To the Editor:—*Does bee venom have any value in the treatment of a patient with arthritis?*

Eugene A. Heilman, M.D., Norristown, Pa.

Answer.—There is no good evidence in the medical literature that any bee venom preparation provides symptomatic relief to arthritic patients with sufficient regularity to conclude that it belongs in the armamentarium of a physician.

SOFT FINGERNAILS

To the Editor:—*What causes fingernails to be soft and rubbery? A patient washes dishes about five hours a day, but he claims that his nails were like this before he started washing dishes.*

Donald R. Gibbs, M.D., Cortland, N. Y.

Answer.—Softening of the nail plate is a rare form of ungual dystrophy. When local causes, such as alkalies and detergents, are ruled out, as in this case, nutritional or metabolic causes must be considered, because the cornification process probably has become defective. Histological study of the nail would not be of diagnostic value. Chemical analysis might give data of real importance, similar to Klauder's finding of disturbance in sulfur content. If such a deficiency is found, topical treatment with sulfur in a penetrating base and a diet high in sulfur would be indicated.

DELIVERY OF SIAMESE TWINS

To the Editor:—*How are conjoined or "Siamese" twins delivered when a cesarean section is not done?*

Alexander J. Kadvany, M.D., Long Beach, Calif.

Answer.—No detailed information can be found in the literature concerned with the delivery of conjoined twins. "Williams Obstetrics" (ed. 11, New York, Appleton-Century-Crofts, Inc., 1956) has the following to say:

> Most conjoined twins (Siamese) are pygopagus; that is, joined back to back with part of the buttocks, sacrum, rectum, and perineum in common. Another common variety is omphalopagus—joined by a single abdominal wall. Dystocia in conjoined twins is rare since most of the union is pliable soft tissue. If any bone is shared it is usually insufficiently ossified at the time of birth to prevent one twin from sliding ahead of the other in the birth canal, the elastic bond being greatly stretched in the birth process.

THROMBOSIS OF RETINAL VESSEL

To the Editor:—*In* The Journal, *June 13, page 215, the answer to the question on thrombosis of retinal vessels contains an astonishing statement: "If, however, the thrombotic vessel happened to be the superior temporal retinal vein (a rare occurrence), one should look for an occluded, pencil-hard temporal artery on that side." My experience, verified by photographs of the fundus, proves that the superior temporal branch of the central vein is the most common side of sudden occlusion, and not a single patient has had temporal arteritis. It is unfortunate that this part of the reply was printed.*

Arthur J. Bedell, M.D.
344 State St.
Albany, N. Y.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Thank you for your comment concerning thrombosis of retinal vessels. The physician from New York is right. The phrase in the answer ("a rare occurrence") is misplaced. It would be advisable to print a restatement.*

The answer to the item entitled "Thrombosis of Retinal Vessel" should have stated, "If, however, the thrombotic vessel happened to be the superior temporal retinal vein, one should not forget to look for an occluded, pencil-hard temporal artery on that side, even though this is a rare occurrence."

WASHINGTON NEWS

Disability Changes Recommended . .
Summary of Poliomyelitis . .
Research Restrictions . .
Welfare Consolidation . .

FLEMMING SUGGESTS CHANGES IN FEDERAL WELFARE AID

Arthur S. Flemming, Secretary of Health, Education, and Welfare, declared that federal welfare aid to states should be in a single package rather than broken up into separate programs.

The administration, he disclosed, is studying a proposal along these lines and may request legislation. However, he said he was not sure this would happen.

At present, the government makes separate grants to the states for old age assistance, aid to dependent children, and aid to the blind and totally disabled.

Without elaborating, the official also said that the administration is working on a program aimed at helping states expand health and welfare services. It is designed to eliminate or reduce dependency due to severe handicaps, he said. Flemming said he hopes such legislation will be ready to present to the next session of Congress.

Flemming made the remarks in an off-the-cuff speech to a meeting of the American Public Welfare Association's national conference.

REPORT ON POLIOMYELITIS

The Public Health Service, noting that 1959 was the worst year for poliomyelitis since 1956, made the following observations about the occurrence of the disease in 1959.

In contrast to recent years, numerous and widely spread concentrations were reported. Three large urban epidemics occurred.

For the past three years, and now in 1959, the preschool age group has had the highest age-specific attack rates.

Unusually high attack rates in Negroes in urban epidemics were observed this year. Such high rates were not noted before 1956.

Type I poliovirus has been predominant in 1959. Small clusters of type 3 cases have occurred. Type 2 has been virtually absent.

Preliminary estimates of vaccine effectiveness indicate that a high level of protection is conferred by the vaccine, especially after four inoculations.

Immunization surveys performed in 36 cities during 1959 pointed to many areas containing poorly immunized populations. These surveys helped direct immunization programs.

Through the 45th week of this year there were 5,150 reported cases of poliomyelitis, of which 71.1% were paralytic. This compared with annual totals of 3,113 in 1958, 2,164 in 1957, and 6,717 in 1956. In 1955, before the Salk vaccine was widely distributed, there were 10,663 cases.

RESTRICTIONS SET ON FEDERAL RESEARCH PROGRAMS

The Department of Health, Education, and Welfare has moved to carry out President Eisenhower's directive that all possible waste be cut from the government's medical research activities.

After Congress appropriated 400 million dollars for the National Institutes of Health for the current fiscal year, the chief executive said that he was concerned about whether the total could be spent wisely. Congress gave NIH, the government's major medical research arm. 259 million dollars more than the administration requested.

Here's how HEW plans to carry out Eisenhower's criteria: 1. The President said that new research should be of such great promise that its deferment probably would delay progress in important research developments.

NIH staffs were instructed to "identify projects for special attention of the advisory councils over and above the review normally given to all projects."

2. New research should not harmfully divert manpower and other resources needed for teaching and medical care services.

NIH will request analyses from those requesting NIH grants on possible diversion.

3. New grants should not substitute federal financing for nonfederal support for medical research and training.

Present grant applications require information on possible diversion of other support. This data will be analyzed and used both in "considering individual applications and in assessing shifts in the total volume of private support."

SOCIAL SECURITY DISABILITY CHANGES PROPOSED

Rep. Burr P. Harrison (D., Va.) announced that he will introduce a bill at the forthcoming session of Congress to liberalize the Social Security program for totally disabled persons.

Major change proposed by the lawmaker, who headed a House ways and means subcommittee that recently held hearings on administration of the disability program, would be to eliminate the present requirement that disabled persons be at least 50 years of age before qualifying for the benefits.

(Continued on next page)

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

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Harrison's bill would have no age restriction. He said the change would add about 100,000 persons to the program immediately, but he predicted the cost could be covered from existing and anticipated surpluses in the Social Security trust fund.

Another proposed change would eliminate the six-month waiting period without benefits now required for qualified totally disabled persons who have unsuccessfully tried to go back to work. Harrison said this "is a good example of a provision which is discouraging people who are receiving benefits from taking the big step toward rehabilitation."

The bill would extend to all types of rehabilitation programs a provision that permits persons to engage in trial work for one year under state and federal vocational rehabilitation projects.

The AFL-CIO had proposed at the hearings that the program, now administered on a federal-state basis, be taken over completely by the federal government. Harrison's measure would leave the present setup unchanged, as spokesmen for the American Medical Association and the administration had requested.

The administration had indicated that it would favor elimination of the 50-year age requirement and was expected to support Harrison's bill.

The disability program, approved by Congress a few years ago, authorizes persons found to be permanently and totally disabled to receive regular Social Security benefits at the age of 50 years rather than waiting until the age of 65 years, provided they are eligible for Social Security benefits.

REPORT ON INFECTIOUS DISEASES

The United States Public Health Service in its weekly report on morbidity and mortality, for Oct. 30 stated that in 1958 there was an increase of about 9% in the number of cases of infectious hepatitis (16,294) over the 1957 figure, (14,922). The number of cases during the last six months of 1958 were about 32% greater than that reported during the comparable period of 1957. In Arizona, there was an outbreak of more than 300 cases on an Indian reservation reported early in the year. The Public Health Service also reported that for the first time since records have been kept the national total number of cases of diphtheria has dropped below 1,000. The total, 918, is 24% less than the 1957 figure of 1,211. The number of cases of typhoid fever (1,043) dropped 15% from the 1,231 cases reported in 1957, and about 40% from the 1,700 in 1956. Almost 20% of cases were reported in California and Texas. Although there was a decrease of 15% in reported cases of syphilis compared with 1957, there was an increase in the number of cases of gonorrhea, leaving the total number of cases of venereal diseases about the same as in 1957.

MISCELLANY

The Department of Health, Education, and Welfare has started a new study of the scientific and legal aspects involved in the use of a synthetic female sex hormone to fatten cattle and poultry. The drug, diethylstilbestrol, is known to cause cancer in the human breast when taken in large quantities, according to the agency. The Food and Dru

Administration stopped issuing new permits for use of the drug after a congressional law banned use of any food additives found to induce cancer; however, there is no authority to rescind permits already issued.

A five-year study on screening and diagnosing glaucoma, one of the most common forms of blindness, has been launched with the financial support of the Public Health Service's National Institute of Health. Techniques currently applied to the detection and identification of glaucoma are now being evaluated at four research centers in this country through grants expected to total approximately $115,000 a year. The grants have been awarded to the Wilmer Institute, Johns Hopkins University Hospital, Baltimore, Md.; Moffitt Eye Hospital, University of California Medical School, San Francisco; Department of Ophthalmology, Washington University School of Medicine, St. Louis, Mo.; and the Department of Ophthalmology, State University of Iowa, Iowa City. The study has four major aims: (1) to define glaucoma in its earliest clinical stages; (2) to develop methods of detecting glaucoma earlier than present diagnostic methods permit; (3) to understand the relation of measurable eye abnormalities, such as increased ocular tension, to the disease; and (4) to evaluate the efficiency of present diagnostic techniques. Since glaucoma seems to be a disease of families, a large proportion of the persons studied will be the children of glaucoma patients.

The Atomic Energy Commission established a 12-member aerospace nuclear safety board on health and safety problems stemming from radioactive matter in the atmosphere. The board, composed of members of the AEC staff, will analyze the effects on health of nuclear space devices and atomic power plants and recommend standards for safe practice.

A one-million-dollar research grant to support a five-year coordinated study of alcoholism in the United States and Canada and to recommend future action was announced by the Public Health Service. The grant was made to the North American association of alcoholism programs.

The House Ways and Means Committee has published the 720-page transcript of the hearings earlier this year on the measure to include health care for the elderly in the social security system. In addition to testimony and statements presented at the time of the hearings last July, the report includes statements submitted later by interested organizations, including state medical societies.

The Department of Health, Education, and Welfare reported that almost 500,000 persons are enrolled in prepaid dental care plans, compared with 123 million covered by hospital or medical insurance. The total for dental plans represented an increase of 150,000 over last year. The HEW Department issued the figures as part of a new pamphlet entitled "Speaking of Prepaid Dental Care: Glossary of Terms."

Virginia became the 40th state to receive a federal grant for participation in the White House Conference on Aging to be held in 1961. Undersecretary of Health, Education and Welfare, Bertha S. Adkins, said that "at the present time, a number of additional state applications are under consideration, and I hope that those states which have not as yet submitted plans or applications will do so in the near future."

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

December

American Association for the Advancement of Science, Morrison Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. of Virginia, Richmond, Va., Director of Public Information.

Association for Research in Nervous and Mental Disease, Inc., Hotel Roosevelt, New York City, Dec. 11-12. Dr. Rollo J. Masselink, 700 W. 168th St., New York 32, Secretary-Treasurer.

New York Heart Association, Symposium on Salt and Water Metabolism, Biltmore Hotel, New York City, Dec. 11-12. Dr. Alfred P. Fishman, N. Y. Heart Association, 10 Columbus Circle, New York City, Chairman.

New York State Society of Anesthesiologists, Inc., Postgraduate Assembly in Anesthesiology, Hotel New Yorker, New York City, Dec. 9-12. Dr. Edwin J. DePolo, 131 W. 11th St., New York 11, Secretary.

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Mid-Winter Clinical Convention for Ophthalmologists and Otolaryngologists (29th), Research Study Club, Ambassador Hotel, Los Angeles, Jan. 17-22. Dr. Norman Jesberg, 500 S. Lucas Ave., Los Angeles 17, Secretary-Treasurer.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal-Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz., Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel, Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oesch Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern Cali Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Bl Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), Univ Texas, Houston, Feb. 25-27. For information write: University o M. D. Anderson Hospital & Tumor Institute, Houston 25, Tex

March

American Broncho-Esophagological Association, Deauville Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Loc Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, C Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Se Treasurer.

American Academy of General Practice, Philadelphia, Mar. Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City Executive Director.

American Association for the History of Medicine, Inc., Cha S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Inst Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broa Colorado Springs, Colo., Mar. 21-23. For information write: Dr. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-P Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hote Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., U Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Tr

American Laryngological Association, Deauville Hotel, Miami Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute o nology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological So Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minn 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., De Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 B Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, real, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emor versity, Atlanta 22, Ga., Secretary.

Missouri State Medical Association, Sheraton-Jefferson Hot Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. L Executive Secretary.

National Health Council, National Health Forum, Miami, Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, tive Director.

National Multiple Sclerosis Society, New York City, Mar. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Ma Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltim Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel, Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave., Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Exec Secretary.

Southwestern Surgical Congress, Riviera Hotel, Las Vegas, Nev., 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral Se Hotel, Mobile, Apr. 21-23. Mr. W. A. Dozier Jr., 19 S. Jackson Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla., 25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Exec Secretary.

American Association of Anatomists, Statler-Hilton, New York Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Med Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Immunologists, Chicago, Apr. 11-15. Calderon Howe, Columbia Univ. College of Physicians and Sur New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists, Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. Holman, of Pathology, L. S. U. School of Medicine, New Orleans, La., Secr

American Association of Railway Surgeons, Drake Hotel, Chi Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chica Executive Secretary.

American College of Obstetricians and Gynecologists, Neth Hilton Hotel, Cincinnati, Apr. 2-6. Mr. Donald F. Richardso Monroe St., Chicago 3, Executive Secretary.

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RELATIONSHIP OF NOXIOUS GASES TO CARCINOMA OF THE LUNG IN RAILROAD WORKERS

Isadore Kaplan, M.D., Baltimore

The medical records of 6,506 deaths among railroad workers included 818 deaths from malignant disease of various organs, and 154 of the deaths were ascribed to primary carcinoma of the lung and/or bronchus. The 154 deaths were classified according to the amount of exposure to exhaust fumes from diesel engines involved in the decedent's actual day's work. The group of workers regularly exposed to diesel exhaust, especially engineers and firemen, proved not to have any higher rate of bronchopulmonary carcinoma than did the nonoperating groups, which included clerks and janitors. Paradoxically, the highest rate was in the clerical group, which also contained a higher percentage of urban as distinguished from rural residents. The place of residence was more significant than the type of work. The cases of bronchopulmonary carcinoma here studied all occurred in men even though about 4% of the employees in the department concerned were women.

THIS study is presented in order to compare primary lung cancer deaths in railroad workers with those in the "non-railroader" public. It analyzes the lung cancer rate of the railroad employees from the standpoint of occupational exposures to noxious gases and air pollutants.

Lung Cancer as an Occupational Hazard

Lung cancer has been recognized for many years as an occupational hazard. The earliest reported case, related to radioactive substances, was in 1879.[1] Farber,[2] in his book "Lung Cancer," said that, in 1935, Lange found that between 60 and 70% of all miners at Schneeberg (Saxony) died of bronchogenic carcinoma due to exposure to pitchblende in the ore. Heuper,[1] head of the environmental section of the National Cancer Institute, mentioned that the total number of Schneeberg miners who died from cancer of the lung between 1879 and 1939 was approximately 400, while the number of Joachimsthal (Czechoslovakia) miners who fell victim to this disease reached 225 between 1926 and 1943. Machle and Gregorius[3] stated that, of 193 deaths in chromate workers, 66 were from cancer, mostly of the lungs. In addition to the uranium and chromate listed above, arsenic, nickel, asbestos, coal tar fumes, and beryllium have from time to time been suspected as lung carcinogens. Today, environmental and experimental studies are being conducted to ascertain the possible role of air pollution by noxious fumes as a carcinogenic factor in the production of lung cancer in human beings.

Medical and Surgical Director, Baltimore and Ohio Railroad Company.

Mortality from cancer of the respiratory system in men in 1956 (20%) was four times as high as in 1930 (5%). Mancuso[4] attributed this rising trend in lung cancer to three factors: (1) tobacco smoking; (2) occupational exposure to carcinogens; and (3) atmospheric pollution. He stated that opinions as to the degree of importance to be attached to each of these factors vary among members of the medical and research professions.

Heuper[1] reported that "three-fourths of the cases of lung cancer in railroad employees occurred among the operating group of workers—a group which represented only 25% of the total number of said employees." The only other related statistical study found in the literature was that of Raffle,[5] who, in 1956, recorded 11 cases of lung carcinoma in London railroad workers during the period 1950 to 1954. He concluded that those deaths did not have any apparent causative relationship to diesel fume inhalation.

Incentive for this statistical study dates from Jan. 8, 1959, when a legal suit was instituted against the Pennsylvania Railroad by one of its disabled machinists, who alleged he had developed cancer of the lung as a result of inhaling diesel shop fumes between 1953 and 1956. From the medicolegal standpoint, this case—which, incidentally, was won by the railroad—indicated a growing belief that inhalation of diesel fume exhausts might be a cause of primary lung cancer.

Source of Material for Study

In view of the paucity of medical information regarding lung cancer in railway workers, the medical records of the Baltimore and Ohio Railroad relief department were used for accurate, unbiased, standardized evaluation. Its employee membership and mortality records for the period from Jan. 1, 1953, to Dec. 31, 1958, were assiduously reviewed and tabulated. Comparisons were made with deaths from all causes and deaths from lung cancer of the nonrailroader public. Statistics were then collated to determine any possible relationship between incidence of lung cancer in various employee groups and their occupational exposure to the noxious fumes.

A total of 6,506 causes of death were reviewed—including 818 deaths from malignancies of the various body organs. All certified transcripts of deaths from malignancies were then inspected. A total of 154 deaths were found to be due to primary carcinoma of the lung and/or bronchus. The causes of these deaths were of significance because a majority of the dead employees had spent the greater portion of their working years at the same position, in engine, train, shop, or clerical service.

Grouping of Railroad Workers

Railroad workers are arbitrarily divided into two different classifications, i. e., the operating and nonoperating groups. However, for the purpose of this study, because they were exposed to varying amounts of noxious fumes in their different occupations, they have been divided into the following three groups:

Group 1 (Operating).—Group 1 employees are directly exposed to exhaust fumes from diesel engines (oil) or steam engines (coal) during operation of trains, locomotives, motors, cars, and all other rolling vehicles. This group is composed of engineers, firemen, motormen, hostlers, road brakemen, yard helpers, yard foremen, conductors, switchmen, yardmasters, and trainmasters.

Group 2 (Nonoperating).—Group 2 includes those members who perform mechanical services or manual labor in either shops or roundhouses. They are exposed, to a lesser degree, to air pollutants from diesel oil, coal smoke, soots, dusts, lubricating oils, and welding fumes. Those included in this group are carmen, carmen helpers, electricians, machinists, boilermakers, blacksmiths, crane operators, stationary engineers, pipefitters, molders, painters, welders, carpenters, crossing watchmen, fireknockers, trackmen, patrolmen, and dump operators.

Group 3 (Nonoperating).—Group 3 employees are rarely occupationally exposed to noxious fumes during the course of their railroad work. This group is comprised of clerks, laborers, janitors, agents, bridge inspectors, and port captains.

The Diesel Engine and Its Exhaust By-Products

Although for many years railroad workers have been exposed to noxious fumes from steam engine (coal) exhaust and various air pollutants in shops, emphasis is now on diesel oil exhaust as a possible carcinogenic factor. The Baltimore and Ohio Railroad initiated its dieselization of locomotives in 1935 and the program was 100% completed in 1958.

The diesel engine was invented in 1892 by Dr. Rudolph Diesel, a German scientist. The first diesel engine–powered locomotive for underground mines was placed in service in the Ruhr coal mining district of Germany in 1927. The diesel engine burns diesel fuel or "fuel oil," which is a hydrocarbon mixture consisting generally of about 85% carbon. Combustion by-products[6] are carbon dioxide, carbon monoxide, sulfur dioxide, nitrogen oxide, and aldehydes (formaldehyde, acetaldehyde, pyruvic aldehyde). In addition to these exhaust products of diesel fumes, the following aromatic polycyclic hydrocarbons have been identified: pyrene, fluoranthene, chrysene, fluorene, 1:2 benzpyrene, 3:4 benzpyrene, and 1:12 benzperylene. Carbon monoxide, nitrogen oxide, and aldehydes, which can be toxic in unusual concentrations, are recognized to be *noncarcinogenic.*

Straub,[7] general claims attorney for the Chesapeake and Ohio Railroad, in 1955 concluded that "in the normal course of railroading, there are only remote possibilities of encountering atmospheres which, together with the time factor, *likely will result in harmful effects.*"

The California Public Utilities Commission[8] in 1956 received a report from the Advisory Committee of the Association of American Railroads on the question of possible hazards to operating crews resulting from exposures to exhaust fumes from diesel locomotive engines. One thousand medical examinations were completed, and "there appeared to be no significant amount of acute health damage and no different experience of those riding in the head engine and the caboose of the freight trains from either the combustion products of diesel locomotives or from the dusts arising out of the use of track sanders."

Kotin and colleagues[9] stated that in a well-operated diesel engine only slight traces of polycyclic hydrocarbons were produced, but by "fuel injection interference" their concentration was increased very considerably and 3:4 benzpyrene appeared. They also mentioned that 3:4 benzpyrene experimentally produced skin papillomas in black mice and skin cancer in strain A mice.

Donovan and co-workers[10] made a survey of the exhaust constituents from a well-maintained diesel engine and found quantities of fluorene, pyrene, and fluoranthene but no 3:4 benzpyrene.

Bailey and colleagues,[6] in their 1959 investigation into the composition of diesel engine exhausts, made this observation: "Most authoritative reports suggest that the contribution of the correctly operated diesel engine is almost insignificant, as far as major harmful pollutants are concerned." They concluded that the principal variable which influences 3:4 benzpyrene production is the fuel flow to the engine and that the exhaust is free of benzpyrene as long as fuel delivery to the engine does not exceed the maker's recommended figure by more than 100%.

Chambers,[11] director of air pollution research, Los Angeles, made the following statement: "All types of vehicles (automobiles and other petroleum-fueled vehicles, except electric-powered) contribute their proportionate share of emissions, but, in most localities, the enormous preponderance of gasoline-driven machines makes the relatively small contribution of diesel, gas, and coal-propelled units quite insignificant, except in the immediate vicinity of their exhaust vents."

Statistical Results and Their Interpretations

In connection with the incidence of primary lung cancer in members of the relief department of the Baltimore and Ohio Railroad between Jan. 1, 1953, and Dec. 31, 1958, the table shows the exposures in each year, with the actual and expected death rate per 100,000.

The method of standardizing the natural death rates for men was as follows:

1. The average relief department membership for each year was determined, and it was then broken into five-year age groups to coincide with the same age groups used by the American Cancer Society.
2. The number in each age group in each year was then multiplied by the death rate per 100,000 reported by the American Cancer Society for the general population for the corresponding age group in the year being calculated and this gave the number of expected deaths.
3. The 154 lung cancer deaths under consideration were likewise distributed by years in five-year age groups, and this produced the actual number of deaths in each year.
4. The total number of the expected and actual deaths, as determined above, was then divided by the exposures (average memberships in each year) to determine the expected and actual death rates for each year.
5. The total number of actual and expected deaths during the six years was then obtained and divided by the total exposures for the six years, thus resulting in the expected and actual death rates for that period.

The larger proportion of deaths from lung cancer occurred in group 3 (clerical), with 89.4% of the expected deaths. Second was group 1 (engine and train service), with 87.5% of the expected deaths. The lowest number of deaths, group 2 (shop), had

*Expected and Actual Number of Deaths from Lung Cancer, 1953-1958**

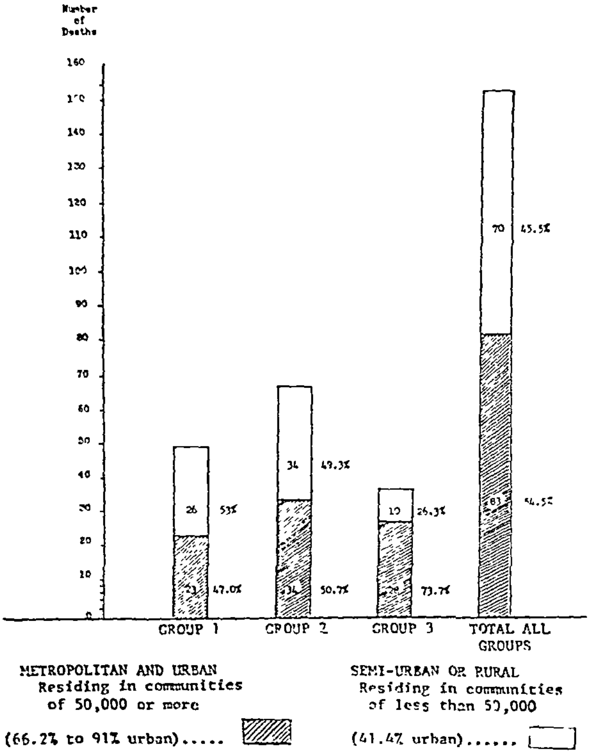
	Group 1			Group 2			Group 3			Total All Groups		
		Deaths			Deaths			Deaths			Deaths	
Yr.	Av. No. of Members	Expected	Actual	Av. No. of Members	Expected	Actual	Av. No. of Members	Expected	Actual	Av. No. of Members	Expected	Actual
1953	13,210	8.209	8	22,930	13.635	12	7,680	6.458	3	43,820	28.302	23
1954	12,360	8.566	6	21,350	14.263	14	7,260	6.688	9	40,970	29.517	29
1955	12,160	8.870	3	20,380	15.012	11	6,890	6.921	4	39,430	30.803	18
1956	12,470	9.860	8	19,820	16.629	11	6,660	7.301	10	38,950	33.790	29
1957†	12,250	10.322	13	18,790	17.183	8	6,410	7.521	7	37,450	35.026	28
1958†	11,340	10.150	11	17,200	16.807	11	5,950	7.635	5	34,490	34.592	27
6-yr. total	73,790	55.977	49	120,170	93.529	67	40,850	42.524	38	235,110	192.030	154
% of actual to expected death rate per 100,000		87.5			71.6			89.4			80.2	
National rate per 100,000		75.9			77.6			104.1			81.7	
Relief dept. rate per 100,000		66.4			55.6			93.0			65.5	

* Based on standardized national death rates and annual relief department exposures for each occupational group.
† Estimated national death rates furnished by American Cancer Society.

71.6%. However, the total of all groups indicated only 80.2% expected deaths, rather than 100%, the national expectancy (basis for standardization).

Comparison of the expected total national death rate of 192 with the actual rate of 154 deaths of Baltimore and Ohio employees implies that fewer employees of the Baltimore and Ohio Railroad died from lung cancer than did a comparable group of the general public. In addition, the number of deaths in group 1, the group with the maximum occupational exposure to noxious fumes, again is less than the norm or expected.

Among our workers, the percentage of deaths from lung cancer in the operating group was not disproportionate to those deaths in the nonoperating group. Percentage of members in group 1 (*operating group*) was 31.4 and in groups 2 and 3 (nonoperating groups) 68.6; percentage of deaths from lung cancer in group 1 was 31.8 and in groups 2 and 3, 68.2. This is in contrast to the figures of Heuper,[1] which indicated that three-fourths of the deaths from lung cancer occurred among the operating group of workers, and this represented only 25% of the total number of said employees.



Residential study of various groups in relation to urban and rural locations.

Significance of Statistics

Careful review of the table and the figure in this paper indicates that the results of the statistical studies are of definite significance. This is especially true for group 2 (shop) workers, who had the lowest percentage of lung cancer deaths (71.6%). In an attempt to discover an explanation for these findings, a study was made of the predeath residences of the 154 employees, and the results are expressed in the figure. It shows almost 50% distribution of the members of group 2 for both urban and rural residences. However, of greater importance is the observation of members in group 3 (clerical), for it indicates that 73.7% of the members reside in urban areas. This may possibly be a factor in explaining the higher percentage of lung cancer in clerks, as compared to other employees.

Of further interest is the realization that all 154 deaths from lung cancer occurred in men, despite the fact that about 4% of the employees of the relief department during that period were women. The majority of women workers in the railroad industry perform clerical duties and, since no deaths from cancer in women are found in this study, it suggests that, if all the women members of the relief department during the years 1953 to 1958, inclusive, were *removed from the study, group 3 (clerical) would* show an even higher percentage of lung cancer.

Finally, it was noted that the average age at death from lung cancer in our workers was 65.1, with 55% of the deaths occurring after the retirement age of 65 years. Apparently their longevity was not affected by the exposure to noxious fumes, since the ages at death in groups 1, 2, and 3 were about the same. However, there was a marked difference between the ages of our decedents from cancer of the lung, as compared to the ages at death of our employees from all causes, since the average for the latter group over the same six-year period was 70.13.

Conclusions

Our *statistical studies fail to reveal any* relation between noxious fumes associated with railroad work and primary lung carcinoma. Ordinarily, one would assume that constant exposure to noxious fumes would produce an increase in lung cancer, but this report did not substantiate this hypothesis. Actually, according to mortality records of the Baltimore and Ohio Railroad relief department, for the six-year period, 1953 to 1958, inclusive, the percentage of deaths from cancer in male employees attributable to primary lung cancer (80%) was actually 20% lower than the expected national percentage (100%).

Evaluation indicates the *inconsistencies* associated with exposure to these noxious fumes. Most deaths from lung cancer were reported in the clerical group of employees, who actually had practically no occupational exposure to the fumes. Paradoxically, those members with the greater exposure to the fumes, namely groups 1 and 2, had less lung cancer than the clerical group.

The study supports the general contention that carcinoma of the lung predominantly affects the male sex, since all 154 cases were in men. Average age at death from carcinoma of the lung was 65.1 years, with 55.2% of the deaths occurring after the age of 65 (retirement age). Carcinoma of the lung among our railroad workers in 1958 showed a continued annual increase, thus paralleling the national trend.

Our records reveal that there is no higher percentage of lung cancer in members of the operating group of railroad employees than in the nonoperating groups, which have lesser exposure to noxious fumes. Railroad workers live predominantly in metropolitan and urban areas (54.5%), compared with rural residences (45.5%). The difference in the two locations is created by the clerical group of employees, 73.7% of whom live in urban areas. This is the group which has the highest percentage of lung cancer in all of our workers.

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CHANGING TRENDS IN CLINICAL INVESTIGATION

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Changing trends in American medicine, medical education, and research have for many years been favorite subjects for messages from chairmen. Nevertheless, since this represents the Centennial Meeting of the Section on Experimental Medicine and Therapeutics, it seems timely to discuss briefly a few of the problems related to the dynamic developments in science in terms of their impact on clinical investigation.

The word "clinical" is derived from the Greek word *klinikos* which means bed; hence, Dr. Fuller Albright pointed out 15 years ago: "Since animals do not sleep in beds, it is quite clear that 'clinical investigation' has primarily to do with the investigation of sick people and is concerned only secondarily, if at all, with sick laboratory animals."[1] One could argue the restrictions imposed by the above statement. Few would disagree that the greatest contributions from clinical investigation have come from success in opening up new knowledge of mechanisms, diagnosis, and treatment of disease in human beings.

Opportunities in clinical research are greater than ever before. Money is relatively plentiful; new institutions have been developed, and the old ones have increased in size. There are many indications that there will be more opportunities for capable men in the future. Yet these developments have created a series of problems which all who are concerned with the vital responsibility of fostering and maintaining productive clinical research must face. Clearly, the primary responsibility will continue to be that of stimulating and recruiting to clinical investigation men with fertile minds who are motivated for research. However, there is little question that recruitment of such men to clinical medicine will increasingly involve competition with many other fields of science.

The astonishing advances in all of the physical and natural sciences have created a peculiarly difficult dilemma for the clinical investigator. He recognizes the unassailable fact that progress in clinical medicine has resulted almost without ex-

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From the University of North Carolina School of Medicine.

Chairman's address, read before the Section on Experimental Medicine and Therapeutics at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1959.

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ception because of previous advances in knowledge in the basic biological, physical, and—more recently—social sciences. As medicine has become more and more a precise science, it has become imperative that the clinical investigator himself obtain a sound knowledge of these basic sciences. It is a common experience for a resident, having completed a long and arduous course of training in clinical medicine, to feel inadequately prepared for a career in clinical investigation, however good his medical school basic science education may have been. Hence, he embarks upon further extensive training in a variety of basic sciences, such as chemistry, nuclear physics, or genetics. Yet this resident is usually well past 30 years of age, beyond the period during which many men, in all fields of endeavor, have historically made their greatest contribution. The difficult decisions he must make re-emphasize the need for hard, critical, and continuing examination of the efficiency of all phases of our American educational system.

This need for further basic scientific training is being met in a number of ways. In many clinical research centers biochemists or physicists have joined the clinical groups. Although the presence of such men in daily working proximity does not lessen the necessity for the clinician to understand the major principles of the basic sciences represented, they can provide for him one means by which he can acquire significant basic principles and facts at the same time he is pursuing the clinical problems which challenge him. Were this movement of basic scientists into clinical groups to proceed at a pace which would seriously diminish the number of persons working primarily in their own discipline, it could create an undesirable effect on the basic sciences from which they come. On the other hand, the increasing number of basic scientists participating in clinical fields demonstrates the fortunate recognition that investigation in clinical departments is rapidly becoming inseparable from that carried out in all areas of biological inquiry. A similar intermingling of learning is evident where, either by design or spontaneously, joint or interdisciplinary groups have developed. In these the members, while retaining their own departmental status, are attacking problems utilizing their combined capabilities. The provision of additional individual training in a basic science laboratory may best fit some men's needs, recognizing the adverse influence of prolonging training mentioned above. A possible favorable by-product of return of the clinically trained men to basic science laboratories could be that some of them would elect to remain in the basic discipline. The loss to clinical investigation would be a gain to the basic medical sciences, where recruitment, at least in some areas, is becoming increasingly difficult.

Reference has been made to the place of animal experimentation in clinical investigation. Should clinical investigators, stimulated by observations on patients, undertake to answer questions by means of well-planned experiments in animals? From one point of view, it could be argued that the clinical investigator should limit his activities to the study of sick people and attempt to persuade his colleagues in the basic sciences to carry out the animal experiments. In practice, except for the occasional fortunate blending of interests in a given institution, this is impractical. I would strongly oppose any such limitation for several reasons. First and most important, such a policy is opposed to scientific principle; the true investigator seeks answers to his questions by using any and all means and techniques available to him. Second, society—scientists and laymen alike—has become increasingly concerned with the perplexity of the legal, ethical, and moral aspects of human experimentation since the terrible events of World War II. The proper place of human experimentation poses a difficult and complex problem for which there is no easy answer.[2] In the context of this discussion, I would submit that uneasiness about the extent to which the human should be the experimental subject is undeniably one reason why one finds in most clinical research centers many more rats and dogs than was true a generation ago. Third—but related to both of the above points—many questions originating at the bedside can be more quickly and accurately answered, at least as applied to the animal species used, by carefully planned and controlled animal experiments than by study of the patient. Some experiments on humans are completely impossible; in others they are indecisive; and in many there is anxiety over the degree of hazard to patients or subjects under study. The recent work of Welt, Oliver, Hollander, Williams, Winters, and others, which clarifies the renal structural and functional lesions of potassium depletion as observed in the rat, provide an example of the precision which is possible by utilization of animal experiments to help answer an important clinical question.[3]

Hence, it seems certain that clinical investigation should and will become more closely associated with the rapid developments in all of the basic sciences. This prediction, however, carries with it certain implications as far as clinical research is concerned. The clinical investigator should remind himself periodically that his primary goals are related to the better understanding and treatment of sick people. The approach is less important than the goal. Solution of a problem may involve moving a great distance from the bedside; if, however, the investigator's activities are in an orbit which eventually provides a better understanding of the original clinical question, I would propose that all phases of his endeavor are clinical investigation. Some persons traversing the orbit may find they can make a greater contribution if they stop permanently at some point removed from the clinic or bedside. Until they make that decision, however, it would appear imperative that they keep their clinical skills sharpened by continuing and regular association with, and responsibility for, patients on the ward and in the clinic. The speed with which their investigation proceeds may not be as rapid as it would be if they dropped their clinical responsibilities, but the unanswered questions in human illness will inevitably be kept in sharper focus. At the same time, too much patient care and clinical teaching responsibility can and does inhibit the productiveness of many clinical investigators. The provision of adequate time and facilities for the competent investigator is a goal which chairmen of most of the clinical departments in medical schools in the United States continually strive for but rarely reach satisfactorily. Similarly, a chairman's attempts to apportion assignments in order to meet all of the pressing service, educational, and research needs of his particular department are usually only partially successful. Clearly, neither unlimited laboratory space nor funds can insure good clinical research; nonetheless, more of both in liberal quantities will help medicine meet the challenge of keeping up with the growing pace of clinical investigation. The relationship of these needs to medical education and care is self-evident. Unless an atmosphere conducive to continued and productive investigation is provided, the quality of medical education must inevitably degenerate.

In summary, although this is an era in which the potential for the further development of experimental medicine and therapeutics is the greatest in history, the full exploitation of this potential will require solution of many problems, a few of which have been discussed here.

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CHEMICAL EVIDENCE OF INCIDENCE OF HYPOTHYROIDISM

STUDY OF EMPLOYED MEN AND WOMEN, PHYSICIANS, AND PROFESSIONAL BLOOD DONORS

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and
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Determinations of protein-bound iodine levels were carried out on serums obtained from 1,823 men in industry, 2,182 male commercial blood donors, 735 male physicians, and 1,015 women employees of a general hospital. The mean for the first group of men was 5.33 mcg.% with a standard deviation of ±1.19; the mean for the women was 5.67 mcg.% with a standard deviation of ±1.22. On the basis of interviews, physical examinations, and laboratory studies on smaller groups of subjects it was concluded that protein-bound iodine values below 4 mcg.% in men or 4.5 mcg.% in women are diagnostic of hypothyroidism. In these four populations, such evidence of hypothyroidism was found in 4.94%, 9.2%, and 4.2% among the men and 7.3% among the women.

Serum protein-bound iodine (PBI) measurement was used to indicate the incidence of hypothyroidism in 1,823 men employed in industry (fig. 1); in 2,182 male professional blood donors (fig. 2); in 735 physicians who volunteered for the test at the Scientific Assembly of the 107th Annual Meeting of the American Medical Association, San Francisco, June 23-27, 1958 (fig. 3); and in 1,015 women employees of the Los Angeles County General Hospital (fig. 4).

Since the thyroxin circulating in the blood provides 98% of the iodine measured as protein-bound iodine,[1] this chemical procedure determines the level of thyroid hormone which circulates in the blood. The inorganic iodine level was determined and reported in all instances. It is usually below 5 mcg.%. Higher concentrations indicate the ingestion of iodide, which may be bound to the serum protein and produce a "falsely elevated" result. A low result may be due to severe hypoproteinemia, as in nephrosis; to the prolonged administration of

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sodium liothyronine (L-triiodothyronine); or to treatment with large doses of testosterone. It is to be presumed that few of the subjects found to have subnormal levels of protein-bound iodine were in the latter categories. Our accuracy with this method of determination of serum protein-bound iodine level has recently been tested.[2] For example, 11 independent determinations on the same serum from this study had the following values: 4.7, 4.9, 5.0, 4.6, 4.8, 5.0, 5.0, 4.8, 4.8, 4.7, and 4.4 mcg.%, with a standard deviation of ±0.19; 95% confidence limits in normal serum were found to be approximately 0.5 mcg.[2]

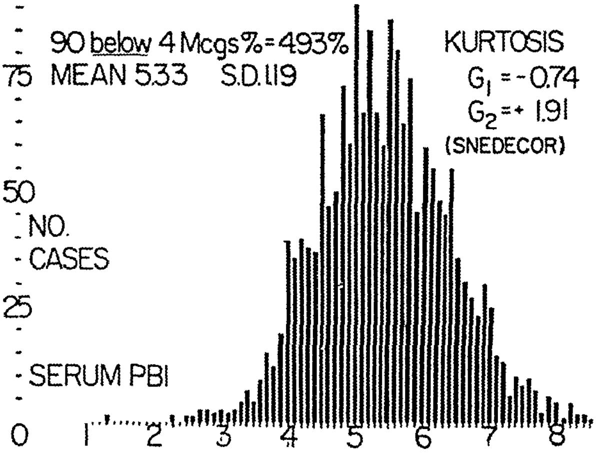

Fig. 1.—Serum protein-bound iodine distribution in 1,823 men in industry; range 1.3 to 8.5 mcg. % inclusive.

Normal Serum Protein-Bound Iodine

The range of normal serum protein-bound iodine level is given by Astwood and associates,[3] Daily and Skahen,[4] Cassidy and VanderLaan,[5] and Peters and Man[6] as from 4 to 8 mcg.%. In their individual series they found that subjects whose level of serum protein-bound iodine was below 4 mcg.% had hypothyroidism. This agrees with the findings in our hospital patient survey which we reported in 1951.[7] We conclude that anyone whose level of serum protein-bound iodine is lower than 4 mcg.% has chemical evidence of hypothyroidism.

Results

The incidence of a serum protein-bound iodine level below 4 mcg.% among the three male groups tested was as follows: 90 (4.93%) of the 1,823 industrial workers (fig. 1); 209 (9.5%) of the commercial blood donors (fig. 2); and 31 (4.2%) of the 735 physicians who had volunteered for the test at the A. M. A. convention held in 1958 (fig. 3).

On the other hand, among the 1,015 female nurses and other female employees of the Los Angeles County General Hospital who had volunteered for the test, only 16 (1.5%) had a serum protein-bound iodine level below 4 mcg.% (fig. 4).

The mean value of serum protein-bound iodine among the male industrial population in our study was 5.33 mcg.%, with a standard deviation of ±1.19 (fig. 1), and in the female employee group 5.67 mcg.%, with a standard deviation of ±1.22 (fig. 4). The calculation of the statistical significance of this difference between these two means results in a possibility of chance of less than one in one [illegible]). Kurtosis calculations[8] were made for each of these populations, and, as expected, it was found that in each of them G_1 was negative and G_2 strongly positive (fig. 1 to 4), thus eliminating the possibility that the distributions might be Gaussian. This indicates that the results are not due to chance and proves that the population is not homogenous.

Clinical Examination

In addition to an interview and physical examination, the laboratory studies done on 64 of the 90 male industrial workers who were available were as follows: repeated serum cholesterol measurement; determination of basal metabolic rate, radioactive iodine uptake, and level of thyroxin-binding globulin; and alpha and beta lipoprotein fractionation by electrophoresis. On the basis of all of these examinations, 3 of these men were considered euthyroid, 21 possibly euthyroid, 20 probably hypothyroid, and 20 definitely hypothyroid.

Assuming that the level of serum protein-bound iodine in the female normally exceeds that of the male by about 0.5 mcg.%, provided the border line between normal and subnormal in the female is placed at 4.5 instead of 4 mcg.%, there were 73 among the 1,015 adult female employees whose level of serum protein-bound iodine was below 4.5 mcg.%. When 32 of these 73 women were interviewed and reexamined, clinical indications of hypothyroidism were found in 80% of them.

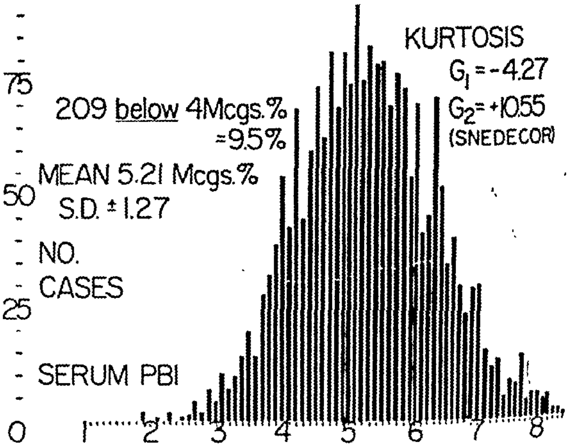

Fig. 2.—Serum protein-bound iodine distribution in 2,182 male commercial blood donors; range 1.9 to 8.9 mcg.% inclusive.

Comment

The present study, with an industrial group three times as large, corroborates our preliminary report,[9] which was based on tests performed on 610 "white collar" workers. In the current study, provided that only men with a serum protein-bound iodine level below 4 mcg.% are included in the subnormal group, about 5% of the group employed in industry have chemical evidence of hypothyroidism. The fact that, in the United States, more than 20 million men in industry fall into this category indicates the possibility that one million American industrial workers are hypothyroid. Among commercial blood donors the number of men whose level of serum protein-bound iodine is below 4 mcg.% is twice as high as in the industrial group.

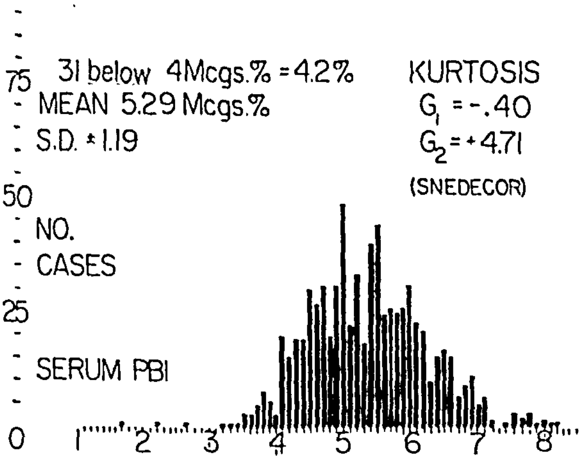

Fig. 3.—Serum protein-bound iodine distribution in 735 male physicians; range 1.7 to 8.4 mcg.% inclusive.

The physicians we tested have a slightly lower incidence of hypothyroidism than the men in industry. Considering that there are 200,000 physicians in the United States, and provided that those attending the 107th Annual Meeting of the American Medical Association in 1958 who volunteered for the test constitute a fair sample, these tests suggest that only 8,000 American physicians have thyroid deficiency.

Of most interest is the finding that the mean level of serum protein-bound iodine is definitely higher in a large group of women than in males. This may be the result of the effect of estrogen on the thyroxin-binding globulin, or it may be due to the change in method of determining levels of protein-bound iodine, although there is no evidence of this. Assuming a higher boundary between normal and hypothyroid, 80% of the women having a level of serum protein-bound iodine below 4.5 mcg.% had clinical indications of hypothyroidism. This suggests that the lower limit of normal in adult females be placed at 4.5 instead of 4.0 mcg.% as for males.

Low Level of Serum Protein-Bound Iodine as Indication for Lifelong Substitution Therapy

Given the normal level of serum protein-bound iodine in males as from 4 to 8 mcg.%, a value of 2.66 mcg. is 50% below the mean found in these studies, 3.20 mcg. is —40%, 3.73 mcg. is —30%, 4 mcg. is —25%, and 4.26 mcg. is —20%. On this basis, guided by our long experience with estimations of hypothyroidism based on the basal metabolic rate, it is recommended that men whose level of serum protein-bound iodine is below 4 mcg.% be regarded as having a serious, permanent thyroxin deficiency which requires lifelong provision of thyroid hormone. This should be given in increasing amounts until the protein-bound iodine, which represents the thyroid hormone circulating in the blood, is maintained at a level ranging from 5 to 6 mcg.%.

Summary

Serum protein-bound iodine (PBI) determinations were done on the following groups: 1,823 men in industry, of whom 4.94% had values below 4 mcg.%, the assumed low limit of normal; 2,182 male professional blood donors, among whom 9.2% had values below 4 mcg.%; and 735 male physicians who had volunteered for the test at the 107th Annual Meeting of the American Medical Association, 1958, only 4.2% of whom had levels of serum protein-bound iodine below normal. Of 1,015 female employees of the Los Angeles County Hospital, who had volunteered for the test, only 1.47% had levels below 4 mcg.%. Statistical comparison of the levels of serum protein-bound iodine of the female with those of the male population indicated that the females had a significantly higher mean level of serum protein-bound iodine, 5.66 mcg.%, with a standard deviation of ±1.22, as against 5.33 mcg.%, with a standard deviation of ±1.19, for the males. It is suggested that a serum protein-bound iodine level of 4.5 mcg.% be accepted as the lower limit of normal in adult females. Subclinical hypothyroidism in American men would appear to exist in about 4 to 5% of the adult male population. Since a serum protein-bound

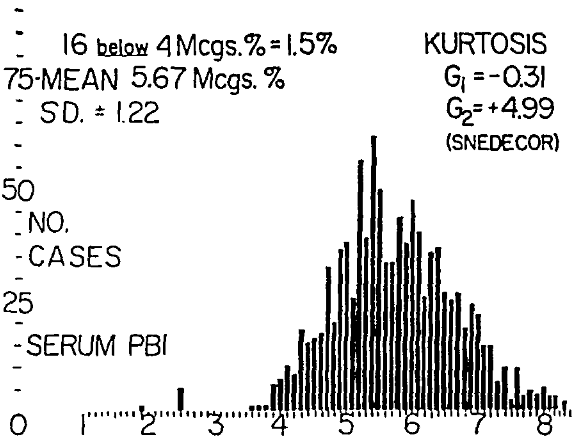

Fig. 4.—Serum protein-bound iodine distribution in 1,015 women employees of a general hospital; range 1.9 to 8.4 mcg.% inclusive.

iodine level of 4 mcg.% is —25% in terms of our mean level of 5.33 mcg.%, it is recommended that men who have values below this be given lifelong thyroid hormone therapy in sufficient daily dosage to maintain their serum protein-bound iodine level at between 5 and 6 mcg.%.

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We wish to extend our thanks to the following persons who were of assistance in providing us with the subjects for our study: the medical directors of General Electric Company, General Petroleum Corporation, Hughes Aircraft Company, Kaiser Steel Corporation, Lockheed Aircraft Corporation, North American Aviation, Inc., Northrop Aircraft, Inc., Richfield Oil Company, Rocketdyne and Atomics International, Southern California Permanente Medical Group, Southern Counties Gas Company, and Union Oil Company; to Dr. John W. Palmer of Hyland Laboratories, Los Angeles, who provided the specimens from professional blood donors; to Dr. Charles E. MacArthur, Chairman of the Section on General Practice, Scientific Assembly of the 107th Annual Meeting of the American Medical Association, San Francisco, June 23-27, 1958; and to Dr. William D. Evans, medical director of Los Angeles County General Hospital, Los Angeles.

We wish to acknowledge the technical assistance provided by Miss Maria Deering and Mrs. Bertha Cook, who made the determinations of serum protein-bound iodine levels for our study.

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PROBLEMS FOR THE RADIOLOGIST IN DIAGNOSIS OF GASTRIC ULCER

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Roentgenographic and fluoroscopic examination of the stomach often reveals ulcers whose nature, whether benign or malignant, cannot be determined from appearance alone. The authors believe that when the nature of an ulcer along the greater curvature and prepyloric areas is in doubt, a two-week to three-week trial of medical management is justified. Reexamination after one or two such trial periods should show substantial healing, if the ulcer is benign. If it is not, surgical treatment is indicated. If a patient with gastric ulcer does not secrete hydrochloric acid even when stimulated with histamine, the probability that the ulcer is malignant is much greater, and immediate surgical treatment is recommended.

The radiologist's problems in the diagnosis of gastric ulcers are largely concerned with the detection of small gastric ulcerations, the determination of the benignancy or malignancy of the gastric ulcer, and minimizing radiation exposure to the patient. The latter problem also raises the question of how often reexamination should be done to determine the progress and healing of an ulcer. Modern medical therapy has introduced new factors in the causation of gastric ulcerations which require his attention. Of prime importance is the induction of gastric ulcers in patients on prolonged corticosteroid therapy (fig. 1, *top*). Of less frequent occurence is the development of gastric ulcerations in patients who have had deep x-ray or supervoltage therapy to the upper part of the abdomen.

Read in the Symposium on Gastric Ulcer before the Joint Meeting of the Section on Gastroenterology and Proctology, the Section on Pathology and Physiology, and the Section on Radiology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

Gastric ulcers may also be a complication of retained foreign bodies such as phytobezoars and trichobezoars (fig. 1, *bottom*).

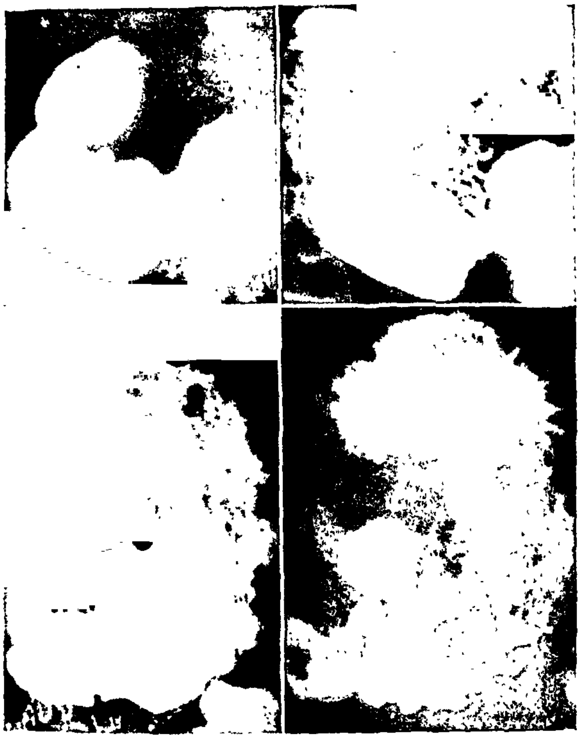

Fig. 1.—*Top* (*left*), acute penetrating prepyloric gastric ulcer induced by prolonged steroid therapy, with (*right*) prompt healing three weeks later. *Bottom*, large penetrating gastric ulcer on lesser curvature resulting from gastric stasis induced by multiple phytobezoars.

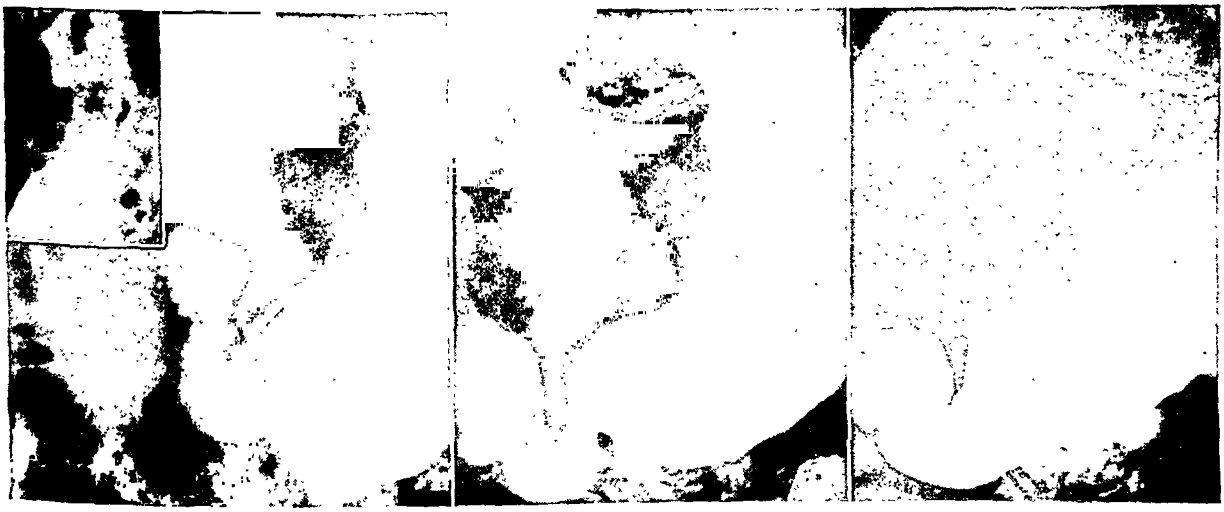

Fig. 2.—Typical acute benign penetrating gastric ulcer in pars media on lesser curvature. *Left*, note demonstration of radiating gastric rugae leading to ulcer crater, indicating a benign gastric ulcer. Roentgenograms made at follow-up examinations, about three, *middle*, and seven, *right*, weeks after institution of medical regimen, showing complete healing of ulcer.

The radiologist's problems can best be organized by dividing all gastric ulcers into three large groups, depending on their roentgenographic appearance: (1) the definitely benign gastric ulcers; (2) the indeterminate group, that is, gastric ulcers that may be either benign or malignant; and (3) the definitely carcinomatous ulcers. The ulcers in group 3 can be quickly disposed of because they are gastric cancers and as such they do not fall within the scope of this discussion.

Method of Roentgenologic Examination

The great majority of gastric ulcers found by roentgenologic examination are benign and fall into group 1. The main problem in patients with this group of gastric ulcers is their early detection and critical evaluation. This requires careful fluoroscopic and roentgenographic examination of the stomach, including a series of "spot films." The examination begins with a study of the gastric mucosa. The patient takes about 2 oz. (60 Gm.) of barium sulfate and is then manipulated in such a manner as to provide a double contrast, with the barium and air used to delineate the pattern of the gastric rugae. This is followed by a detailed study of the gastric mucosa, with use of compression to spread out the gastric rugae and to press barium into any shallow ulcer crater. Fluoroscopic examination of the barium-filled stomach is employed with manual palpation to visualize the entire contour, thus revealing any ulcers to the best advantage both in profile and *en face*.[1] The examination is concluded by filming the stomach in the anteroposterior, lateral, and oblique projections, with the patient in both erect and horizontal positions. Delayed films are valuable in determining gastric emptying and gastric motility. Some gastric ulcers may even be more apparent on the delayed film, as pointed out by MacMoran and co-workers.[2] Only after these measures have been employed can the patient be said to have received a competent and thorough roentgenologic examination. This can be accomplished efficiently, without causing excessive radiation-exposure, by a physician trained in radiology.

Almost all ulcers in the proximal three-fourths of the stomach can be demonstrated in silhouette, (fig. 2 and 3). Those on the posterior and anterior walls of the antrum and the prepyloric and pyloric areas are best shown by compression technique, since they usually cannot be placed in profile (fig. 4). Fluoroscopic image intensification units have been useful in minimizing radiation exposure from fluoroscopy but have not added materially in the detection of most ulcers. One rule that has proved helpful is to repeat an examination which has given an initially negative result, if the patient's symptoms persist without a satisfactory explanation. Such conditions as patient relaxation, state of hydration, gastric secretion, and fluid retention may change in the interval between examinations, and these alterations may make the ulcer more demonstrable. Another point worth emphasizing is that 15% of patients with gastric ulcers also have a duodenal ulcer.[3] Gastric ulcers associated with gastric hypotonicity are more difficult to demonstrate in patients with hypomotility and retained gastric secretions.[4]

Criteria for and Management of Malignancy

While we believe that we are still finding about five times as many duodenal ulcers as gastric ulcers, we have the impression that gastric ulcers are seen more frequently. Gastric ulcers are still reported as occurring in about the same location and at about the same frequency; about 2% in the c and fundus, 65% in the pars media, 15% in th trum, 10% in the prepyloric area, 2% in the mus, and 6% along the greater curvature.[5]

The incidence of simultaneous occurrenc multiple gastric ulcers[6] is increasing from time-honored figure of about 2% to about 6% 5). This is probably due to the increased effici of the roentgenologic examination in the tection of smaller lesions. Katz and Bierenba in a review of cases of multiple gastric ulcers pressed the belief that gastric ulcers are be when they are multiple and are only occasio associated with carcinoma.

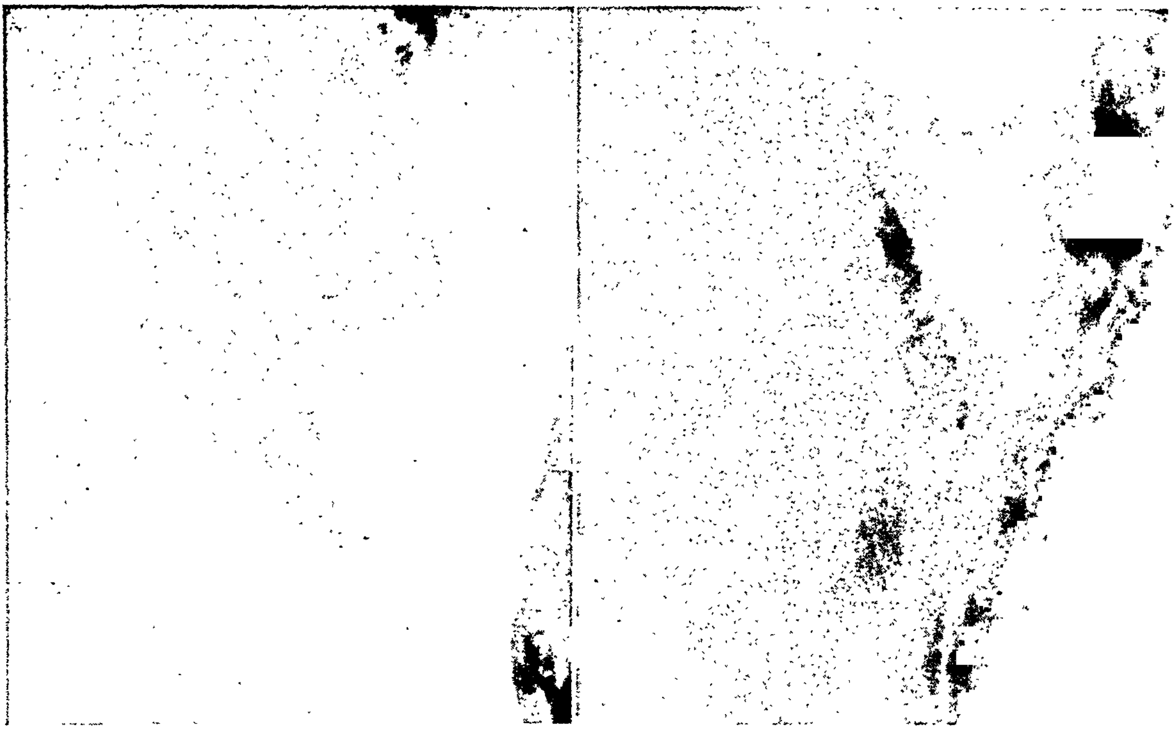

Fig. 3.—*Left*, large penetrating gastric ulcer on lesser curvature, with, *right*, marked decrease in size and evidenc healing within three weeks. Final roentgenologic examination should be made to demonstrate complete healing, to be cer that no malignant change has occurred.

Reports[7] are accumulating that have alte current thinking about malignancy of gastric ul along the greater curvature of the stomach. It n appears that about half of them are benign, whe as not long ago they were considered "maligna until proved otherwise." This same attitude prevailed for many years with regard to gast ulcers in the prepyloric area and in the isthm yet we are now seeing reports which indicate t this may or may not be so. Elliott and co-workers in their study of ulcerating lesions of the stoma found that "there is no statistical evidence lendi credence to the dogma of 'malignant until prov otherwise' when an ulcer is either large in size located in the prepyloric area or along the great curvature of the stomach. Instead it would appe that there is at least an even statistical chance that these lesions will be benign." These and similar statements by others indicate that location and size of the ulcer are no longer valid criteria in themselves for determining whether an ulcer is malignant.

Do these statements mean that gastric ulcerations have become less malignant? No; we believe that this is due to an improvement in the radiologist's ability to recognize gastric cancer and also to the gastroenterologist's and the internist's abilities to distinguish malignant from benign gastric lesions. Without a doubt, all physicians have developed a better understanding of both of these conditions during the past decade.

Assuming these new concepts to be true, are we then justified in advocating the same short trial period of medical management for ulcers along the greater curvature and prepyloric areas as we have for those in the pars media? We think it is justifiable to apply this form of management. The size of the ulcer has little importance in cases selected for medical management. We must, however, take into account the greater cicatricial changes that occur in the prepyloric antrum with healing and realize that about 20% of them will eventuate in pyloric obstruction. We would therefore recommend confirmation of the roentgenologic diagnosis of the benign gastric ulcer and of ulcers in the indeterminate group by applying this trial regimen, with reexamination in two to three weeks. If the lesion is definitely smaller, the medical regimen may be continued for another three-week or four-week period. Most benign ulcers will have healed in this interval. It is desirable to repeat the roentgenologic examination of the stomach a third time to be certain that complete healing has occurred. If, after application of this therapeutic regimen, reexamination shows that healing is incomplete and there is not complete relief of the patient's symptoms, then surgical treatment is indicated. The therapeutic regimen must be applied much more rigidly to any patients with recurrent ulcers, since the rate of malignancy is much higher in this group.

In actual practice, we have found it difficult to persuade the patients to come back for the third examination and even sometimes for their second examination, because they begin to feel so well that they do not see the necessity for the final study. The subsequent examinations do not have to include the entire upper gastrointestinal tract and can be limited to the stomach and performed at a lower cost and with less radiation exposure.

To summarize, the medical regimen test and serial roentgenologic reexamination showing definite evidence of healing constitute the most reliable means of determining that a penetrating gastric lesion is benign. An exception to this rule may be the patient with histamine-fast achlorhydria; these patients are five times as apt to have an associated malignancy and may need immediate surgical treatment. When the possibility of malignancy cannot be dispelled, despite all appropriate laboratory and therapeutic tests, surgical measures become mandatory.

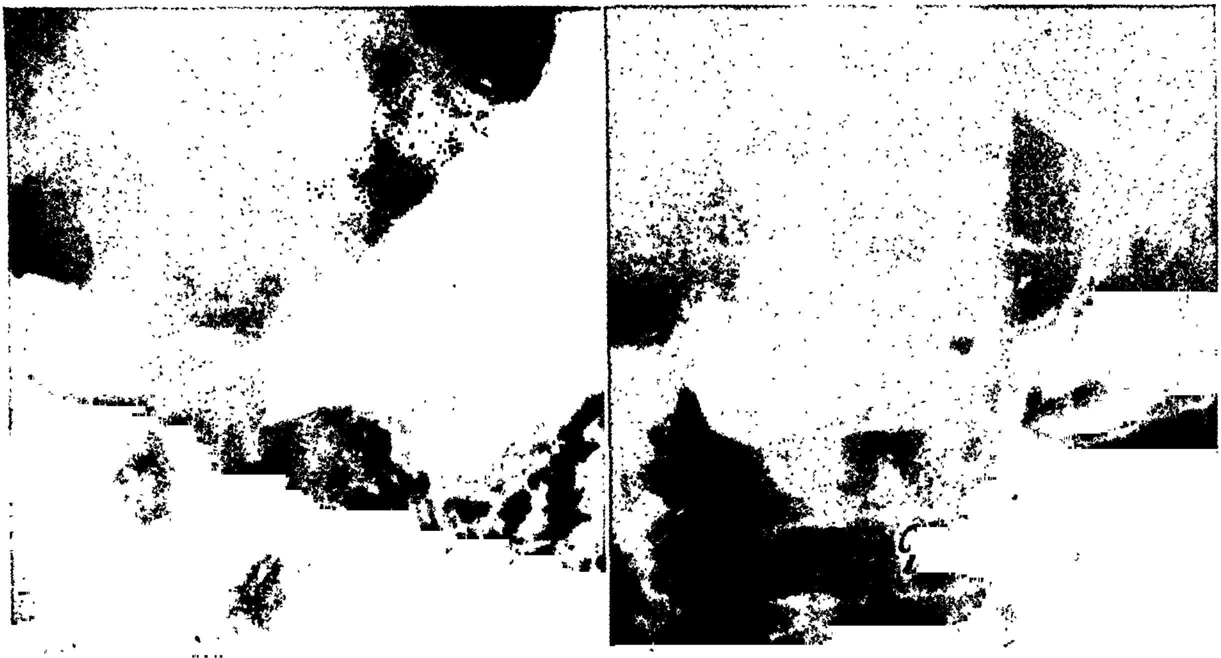

Fig. 4.—*Left,* acute penetrating gastric ulcer in antrum of stomach on posterior wall demonstrated by pressure technique, with, *right,* complete healing in about two and one-half months of treatment by medical regimen.

When this practice has been followed, what has been the percentage of error? Elliott and co-workers[7a] reported a 20% excess in overdiagnosing "malignant" or "probable malignant" disease and an error of 6% of malignancies diagnosed as "benign" or "probable benign." This 6% error compares favorably with the accepted roentgenologic margin of error in attempting to distinguish between benign and malignant gastric lesions. Peterson[8] at the University of Minnesota, following a similar practice. has done even better, with a reported 3% error. The 20% overdiagnosed as possibly malignant indicates that "when in doubt" they have been erring on the side of malignancy.

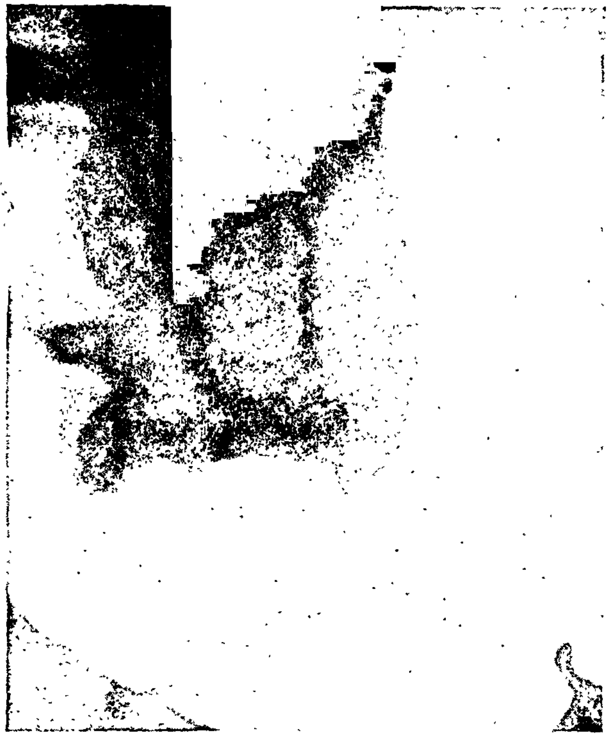

Fig. 5.—Patient with two small gastric ulcers on lesser curvature of pars media and one at pylorus. Multiple gastric ulcers occur more frequently than previously considered. It is also well to keep in mind that 15% of patients with gastric ulcers will also have duodenal ulcers.

The roentgenologic criteria for benignancy in the diagnosis of gastric ulcer depend on several well-established attributes, none of which is pathognomonic. Among them are (1) protrusion of the ulcer crater beyond the stomach wall, with the demonstration of a smooth ulcer floor and contour; (2) demonstration of mucosal folds radiating into the ulcer crater; (3) demonstration of a narrow band of translucency about the neck of the crater formed by a collar of overhanging mucosal edges (Hampton's line) (fig. 3); and (4) absence of induration around the base of the ulcer, with pliable adjacent stomach wall and persistence of peristaltic movement through the area of ulceration. Usually two or more of these characteristics form the basis for the diagnosis, but each lesion is an individual problem and must be evaluated on its own merits and appearance.

Conclusions

In conclusion, from the radiologist's experience the following statements concerning gastric ulcers appear justifiable: 1. More gastric ulcers are being found, a fact due perhaps as much to more efficient roentgenologic examination as to rising incidence. 2. Gastric ulcers are not infrequently multiple in occurrence. 3. The most significant diagnostic roentgenologic finding is the demonstration of an ulcer crater into, or through, the stomach wall. 4. An adequate trial of medical management is almost always indicated, followed by a roentgenologic re-examination to demonstrate complete healing. If this is not feasible, then a surgical approach might be considered at the onset.

5. With regard to the relationship of gastric ulcers to gastric malignancy, the incidence of malignancy in the gastric ulcer which appears benign on roentgenographic examination is extremely low —approximately 3%[8] to 6%.[7a] The incidence of mortality from gastric resection by the average surgeon is probably as high as or higher than the error by the average radiologist. There are no roentgenologic findings which absolutely exclude the possibility of malignancy. The size and location of the ulcer cannot be related to the presence or absence of malignancy. Likewise, these factors have little importance in the selection of cases for medical management. The most reliable and practical method of establishing the diagnosis of a benign gastric ulcer is to institute the therapeutic regimen together with a roentgenologic examination after two weeks, with the demonstration of progressive healing. There is no simple practical clinical test for determining the presence or absence of malignancy in an ulcer.

The radiologist's problems in the diagnosis of gastric ulcers were well summarized by Dr. Leo J. Rigler[9] in 1935 when he wrote, "On the shoulders of the general practitioner lies the responsibility of recognizing the seriousness of gastric symptoms of patients in middle age and of urging early and repeated x-ray examinations.

"Upon his shoulder also rests the responsibility of seeing to it that the roentgenologic examination is done by one who is most competent in the art—otherwise, it may be worse than useless. Upon the shoulders of the radiologist rests the responsibility and also the opportunity of making the diagnosis early and distinguishing it from carcinoma of the stomach so that surgical treatment may have some opportunity for success."

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CONTRIBUTIONS OF THE PATHOLOGIST TO PRESENT-DAY CONCEPTS OF GASTRIC ULCER

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Gastric ulcers in 243 patients, all of whom were 50 years of age or older, were studied by autopsy procedures, and the data were correlated with some of the presumptive factors in the differential diagnosis of gastric ulcer. The teaching that the benign types of ulcer occur more commonly than those of neoplastic origin was upheld; a 3-to-1 ratio was found to exist and to extend to the 80-year-old group of patients. Classification of ulcers by size and type gave the following information: 10% of the benign ulcers were 4 cm. or more in diameter and 20% of the malignant ulcers were 2 cm. or less in diameter, but in the 53 ulcers larger than 4 cm. the number (33) of neoplasms was greater. No differential diagnostic values could be assigned to the location of the ulcer on the stomach wall. Transformation from a benign to malignant lesion was calculated to take place in less than 1% of peptic ulcers.

While the pathologist has many roles to serve, one of the more important contributions he may make is to reassess periodically his knowledge of the more unsettled issues in medicine. Peptic ulcer, particularly gastric ulcer, is an entity which remains shrouded in many enigmas. Moreover, even our slender fund of knowledge on this subject is riddled by contradictions and confusions. Much that has been said about this subject is controversial, and certain aspects have been overemphasized.

I should like critically to reexamine four points with respect to gastric ulcers: (1) the significance of the age of the patient in the differential diagnosis of benign and malignant gastric ulcer; (2) the significance of the size of the ulceration in the determination of whether it is benign or malignant; (3) the value of the site of the ulcer as a point of differentiation between benign and malignant lesions; and (4) the hazard of the transformation of a benign peptic ulcer into a gastric malignancy.

Materials and Methods of Study

To evaluate these four points, a study was made of 234 cases of gastric ulceration at the Mallory Institute of Pathology of the Boston City Hospital, during the years 1940 to 1949. This included all cases of gastric ulceration, benign and malignant, that occurred consecutively during these years in

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patients 50 years of age or over who came to autopsy in this institution. It therefore represents a largely unselected population that more or less exemplifies the incidence of these lesions in the population of a large municipal hospital. Patients over the age of 50 years were selected for the reason that it is often said that a gastric ulcer is more ominous in patients in this age group, because older patients are so much more likely to have a malignancy than are younger patients. While these data were taken only from postmortem specimens, it was felt that such a series would, if anything, have a higher incidence of malignant lesions, since benign lesions might have healed and not be represented in this study; and, moreover, since the hospital accepts a great many patients for terminal care, terminal gastric malignancies would have a slightly higher incidence in the final distribution. This higher incidence of malignant gastric ulcer was completely acceptable, however, since it was believed from previous experience that this weighting would only serve to emphasize the points to be made.

TABLE 1.—*Age at Death of 234 Patients with Benign and Malignant Gastric Ulcers*

		Ulcers			
		Benign		Malignant	
Age Group, Yr.	Total	No.	%	No.	%
50-59	48	40	83.3	8	16.7
60-69	80	52	65	28	35
70-79	81	58	71.6	23	28.4
80 and over	25	18	72	7	28

It can be seen from table 1 that, even in this advanced age group, with such weighting as may have occurred on the basis of the data already given, in each decade benign gastric ulcers are far more common than malignant ulcers. These data merely emphasize the fact that benign peptic ulceration is more common at all ages than is malignant ulceration of the stomach, and that even in the advanced age groups, 80 years and over, the ratio remains almost three to one, benign to malignant.

The data in table 2 show clearly that, when the benign ulcers are classified according to size, about 10% of all benign lesions are over 4 cm. in size. Conversely, about 20% of malignant ulcers were less than 2 cm. in diameter. The belief, stated many years ago, that a large ulcer is almost always malignant is therefore proved to be incorrect. Considerable emphasis has been placed on the differential importance of the 4-cm. size of the crater. However, it must be appreciated that this differential importance is only relative. It is true that when ulcer craters of 4 cm. and over were analyzed it was seen that there were 20 benign as against 33 malignant lesions in patients in this series. It is therefore perfectly true that in a given patient there is still a more than even chance that a 4-cm. lesion will be malignant, but it must not be forgotten that it may still be benign and, moreover, that the small gastric crater may well represent a malignancy. I should emphasize that even these small malignant ulcers were, in most instances, the primary cause of death of the patient; and all physicians, I am certain, have had the experience of seeing a small ulcerative carcinoma lead to metastases before the primary lesion has caused significant symptoms.

With respect to the site of gastric ulceration, it is evident from the following data that there has also been too much emphasis on the differential value of the location of the lesion. The site of an ulceration has been classified in two ways in table 3.

First, the stomach was divided into the so-called pyloric and prepyloric areas (included together under the heading prepyloric) and then into body and cardia as major subdivisions, and then these same ulcers were reclassified with respect to their location on the curvatures or anterior or posterior walls.

Only those lesions which were well confined to one of these geographic areas were included in this analysis. In this group 58% of all benign lesions occurred in the pyloric-prepyloric region, and 56% of all malignant lesions occurred in the same location. In terms of absolute numbers, the figures indicate that there were 87 benign to 34 malignant prepyloric ulcerations in a consecutive postmortem series. Prepyloric location, therefore, is not indicative of malignancy; in fact, on the pure basis of chance and probability there is at least a two-to-one likelihood that a lesion in this location will be benign. With respect to the classification of ulcerations on the curvatures, it is evident that 14% of all benign lesions occurred on the greater curvature and 39% of all malignant lesions on the lesser curvature. In fact, with respect to location on the greater curvature, the absolute figures reveal 24 benign and 23 malignant ulcers. As one would anticipate, in terms of lesions located on the lesser curvature, the figures are 78 benign and 33 malignant ulcers. Once again the data indicate overemphasis on the seriousness of location on the greater curvature and also indicate that ulcers on the lesser curvature may indeed be malignant, in our present series the proportion is again almost one-third malignant of all lesions on the lesser curvature. However, it must be remembered that

TABLE 2.—*Analysis of the Size of 190 Benign and 68 Malignant Gastric Ulcers*

	Ulcers			
	Benign		Malignant	
Diameter, Cm.	No.	%	No.	%
1 or less	65	34.2	3	4.4
1.1 to 2	62	32.6	11	16.2
2.1 to 3	24	12.6	9	13.2
3.1 to 4	14	7.4	9	13.2
4.1 and over	20	10.5	33	48.5
Unknown	5	2.6	3	4.4

these absolute figures do not necessarily reflect the true incidence nor the true distribution of these lesions in the entire population, since the figures are undoubtedly weighted by the facts that an older age group was dealt with and that the healed benign lesions were not analyzed, and by other factors as well. These data merely indicate that there are no absolute differential values to the location of an ulcer.

The possibility that a benign peptic ulcer may become malignant has, I believe, been overemphasized. The variable opinion expressed in the literature is in large part a reflection of the variable criteria used by the authors of various studies. It is at best difficult to determine whether a gastric carcinoma may have indeed arisen within a preexisting peptic ulcer. It must be remembered that gastric carcinomas of all varieties may undergo peptic digestion, particularly in a stomach having a highly corrosive acid peptic juice. It is therefore possible for a preexisting gastric carcinoma to assume the appearance of a previously benign peptic ulcer. Such a lesion may therefore be interpreted as malignancy arising in a previously benign process. At the Mallory Institute the criterion has been adopted that if malignant invasion is found in the base of an ulcer as well as in the margins and walls of the ulcer it is more likely true that the lesion represents a preexisting carcinoma arising "de novo." In the rare case in which malignant transformation is believed to have occurred in a benign peptic ulcer, the cancer is generally confined to the mucosal margins of the ulceration, without involvement of the base.

It is true, however, that if the progress of these lesions is followed long enough they will directly invade the entire wall of the stomach and involve the base as well, but at this point it would be impossible to recognize the preexistence of a benign process. It therefore seems unwise to make judgments in patients with far-advanced malignancies, because the landmarks are so obliterated as to make the trail impossible to follow. With the aid of the criteria just set forth it is my contention that malignant transformation occurs in less than 1% of benign peptic ulcers arising in the stomach. I might add a word of caution; the history of a patient's having had an ulcerative process for many years does not indicate that the lesion must have been benign for a long period, because, once again, one encounters undoubted carcinomas that have followed a relatively benign course for years, and there is no precluding the possibility that a patient may have had a benign peptic ulcer that healed only to be followed after some period by a malignancy arising in a totally different site.

TABLE 3.—*Classification of Ulcer Status by Location*

Ulcers	Prepyloric	Body	Cardia	Greater Curve	Lesser Curve	Anterior Wall	Posterior Wall
Benign	87(58%)	52(35%)	11(7%)	24(14%)	78(47%)	21(13%)	44(26%)
Malignant	34(56%)	19(31%)	8(13%)	23(27%)	33(39%)	10(12%)	19(22%)
Total no.	121	71	19	47	111	31	63

Summary

A fresh look at the problem of the differential diagnosis of the gastric ulcerative lesion indicates that even in patients of an advanced age the probabilities are in favor of a lesion being benign on the sheer basis of the frequency of the two kinds of diseases. Size is not of absolute differential value, and location has been grossly overemphasized as an important criterion, as has been the hazard of malignancy developing in a previously benign peptic lesion.

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VIRUSES, INFECTIONS, AND DISEASES.—The older idea of "one disease-one agent" has had to give way to the concept that a well-defined clinical syndrome may be induced by any one of a number of viruses and that one virus may induce several different symptom complexes. The new knowledge has important implications to understanding viral infections of the respiratory tract. As an example, the clinical syndrome called influenza may be induced by some ten or eleven different viruses, only four of which are designated as influenza viruses. Moreover, one influenza virus may induce a wide variety of clinical entities ranging in severity from very minor upper respiratory infections to fatal viral pneumonia. Thus, a diagnosis of influenza may mean quite different things to the clinician and to the virologist. Ideas about viruses, like those about bacteria, are becoming less and less disease-oriented and more and more concerned with the mechanism of infection which may, but more commonly does not, lead to disease.—Frank L. Horsfall Jr., The J. Burns Amberson Lecture, *The American Review*, September, 1959.

SURGICAL MANAGEMENT OF GASTRIC ULCER

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and
William R. C. Stewart, M.D., Columbus, Ohio

Whether a given gastric ulcer is benign or malignant can be decided only by the pathologist examining the excised specimen. In a series of 155 patients hospitalized with the diagnosis of gastric ulcer, agreement between physician and surgeon that the ulcer was benign occurred in about 7% of the cases. In 5% of the patients the ulceration is believed to have been precipitated by gastric irritants and stimulants, such as medicaments taken habitually. Medical management, including withdrawal of such irritants, should be tried; if this fails a surgical program adapted to the location of the lesion is recommended. The postoperative course of patients with conservative forms of gastric resection was compared with that of patients after radical resections. In a series of 76 patients those with conservative resections were underweight in 42% and troubled with moderate or severe dumping symptoms in 2.6% of the cases, while the corresponding figures for radical resections were 80% and 47%. Routine radical resection for gastric ulcer is not justified by the known incidence of malignancy. Hope lies in better diagnosis and in earlier, rather than more radical, surgery.

The discouraging results in the treatment of gastric carcinoma over the years have suggested the need for more aggressive management of gastric ulceration. So many of the old diagnostic stand-bys have failed just often enough in differentiating a benign from a malignant ulcer to strengthen the surgeon's conviction that early surgery is the logical solution.

While gastroscopy[1] and exfoliative cytological studies[2] have confirmed malignancy in many cases of so-called benign ulcer, most patients in the United States are treated without these added diagnostic facilities. However, regardless of how extensive the studies, the brutal truth remains that every gastric ulcer may be a cancer. Only the pathologist, with the surgically excised ulcer available in his laboratory for microscopic study, can tell for certain whether a particular ulcer is benign or malignant.

It is believed that a more aggressive policy might be developed if a "cancer type" of radical resection were not routinely performed for both benign and malignant lesions. Certainly the patient would benefit. A comparison of our experience, over a five-year period, with routine radical resection for gastric ulcer to that, in a recent three-year period, with more conservative resection has convinced us that the conservative approach is desirable.

Incidence of Unsuspected Malignancy

As in patients with duodenal ulcer, intractable pain, hemorrhage, and obstruction as well as perforation remain the standard indications for surgery. Despite a disagreeably high incidence of recurrence, the physician has relied on medical therapy for uncomplicated ulcers; this is because the odds may be as favorable as 10 to 1 that a well-studied gastric ulcer is benign. He is loath to recommend operation, since he has been more impressed with the disagreeable side-effects of radical resection for what turned out to be a benign lesion than he has been by missing a diagnosis of carcinoma of the stomach.

The physician might favor early surgery more if the surgeon could show overwhelming evidence that early operation for gastric ulcer insures a higher five-year survival rate of patients with gastric malignancy. This is suggested from the experiences of Hayes[3] and Ravdin.[1] In contrast, the surgeon has been pleased with the results of even the most conservative procedures for benign gastric ulcers because of the low incidence of marginal ulceration as compared with duodenal ulcer.

Most patients cooperate medically when threatened with the removal of a large part of their stomach, but they also become increasingly alert to the potential of malignancy. As a result, they resist the idea of prolonged diet and hospitalization.

Continued confidence in the medical treatment of gastric ulcer was apparent from a review of 155 patients hospitalized with this diagnosis during the years 1956 to 1958 inclusive. During this period 42% of the patients with a diagnosis of gastric ulcer were not seen in consultation by the surgeon. Slightly over one-fourth, or 28%, of the patients were subjected to a gastric resection, while in 30% surgery was delayed for a variety of reasons.

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Read in the Symposium on Gastric Ulcer before the Joint Meeting of the Section on Gastroenterology and Proctology, the Section on Pathology and Physiology, and the Section on Radiology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

There was general agreement between the physician and the surgeon in approximately 7% of the cases that the ulcer apparently was benign. A longer period of bed rest and intensive therapy was recommended. Although three weeks of hospital treatment has been referred to over the years as the classic trial by medication, it is doubtful if this magic figure is followed generally. As a matter of fact, it is more likely that economics makes it mandatory that many patients remain ambulant and that medical treatment be continued much longer. In 6% of the patients in the present series the immediate surgery was not recommended because of the patient's age or an advanced cardiac condition: these made the dangers of malignancy less than the dangers associated with gastric resection. Another 3% refused surgery. In 5% of the patients gastric irritants and stimulants were believed to have precipitated the ulceration. A program of drug withdrawal and intensive medical therapy was agreed on.

The possibility of a drug-induced ulcer from the ingestion of gastric irritants or stimulants is assuming greater importance in these days of the "coffee break."[5] Furthermore, as the age of the population increases, the incidence of arthritis mounts and relief is sought by self-medication with salicylates and other arthritic "pain-killers." We have been impressed by the number of patients who accept self-medication as so routine that even under close questioning they neglect to mention it. The effect of salicylates, phenylbutazone, and steroids on the upper gastrointestinal tract is well known.[6] On occasion, antihypertensive drugs such as reserpine[7] deserve consideration if the patient's difficulty coincides with the administration of this particular medicament. Finally, excessive use of alcohol would be a strong deterrent to early operation in a given patient.[8] However, the possibility of malignancy is ever present.

It is of the utmost importance to evaluate the probability of malignancy in every patient with gastric ulceration. When malignancy is suspected early operation is mandatory. A strong indication for surgery is the combination of persistent symptoms and roentgenologic evidence of an ulcer despite intensive medical therapy. Relatively few patients would be subjected to gastric resection after a short period of ambulant medical treatment unless they were having so much distress that the relief of pain would be an indication for surgery. When exfoliative cytological studies show suspicious cells in gastric washings, early surgery is mandatory. Patients with these findings should not be included in the statistical study of questionable cases.

The radiologist's opinion about whether the gastric ulceration has the characteristics of malignancy plays a major role in the decision for or against surgery. He should be given the opportunity to restudy the patient if there is any doubt of the diagnosis. If surgery is delayed, the patient's progress must be followed by interval roentgenologic studies. Histamine achlorhydria certainly should be an influencing factor; however, high free acid values do not exclude malignancy. The increasing incidence of gastric cancer in the presence of pernicious anemia is well recognized, and any gastric ulceration occurring in such patients should be resected. The same principle would apply to the patient with a recurrent crater.

If an ulcer is located on the greater curvature or in the body of the stomach the probability of malignancy rises. Of less significance, perhaps, is the location of an ulcer in the prepyloric area. Finally, the value of gastroscopy in influencing the indications for surgery depends more on the ability of the gastroscopist than on any other factor. It must be remembered that the priority of these influencing factors varies with the individual case. Certainly, a combination of several of these provides strong evidence of malignancy.

Many times it is difficult to determine the optimum time for surgery when the evidence favoring malignancy is minimal. In contrast, there is little disagreement about the indication for surgery for emergency complications such as massive hemorrhage, free perforation, or persistent obstruction of the stomach. The complications occurring in gastric and duodenal ulcer are handled in the same manner, but it is advisable to perform biopsies on all gastric perforations.

Conservative Versus Radical Surgery

Like others,[9] we have been impressed with the number of patients with a history of duodenal ulcer. It is important to investigate the type of surgical procedure which may have been carried out previously on the stomach or duodenum. On occasion, previous surgery for duodenal ulcer such as vagotomy with inadequate drainage of the antrum, resulting in a prolongation of the antral phase of secretion, was no doubt responsible for subsequent gastric ulceration.[10]

A survey of surgical experience with gastric ulcer over a six-year period ending in 1955 has been reported by Denkewalter and Watman.[11] During that period a radical gastric resection of 70% or more, to insure removal of the immediate lymphatic drainage area, was routine for any patient operated on for gastric ulcer. They concluded that this approach was too radical, since 80% of the patients had a large part of their stomach unnecessarily sacrificed for a benign lesion. They advised proof of malignancy by biopsy and immediate frozen section before such a radical procedure was performed. During that six-year period 34% of all patients with gastric ulcers admitted to the hospital were operated on. An unsuspected malignancy was found in 9% of these patients.

After these studies we have altered our plan of treatment during the past three years, 1956 to 1958 inclusive. During this three-year period 30% of patients were operated on, with the unsuspected finding of malignancy in 11%. Over both periods of study, which comprised a span of eight years, one in every three patients admitted to the hospital with gastric ulcer underwent gastric resection. Unsuspected malignancy was found in approximately 1 in 10.

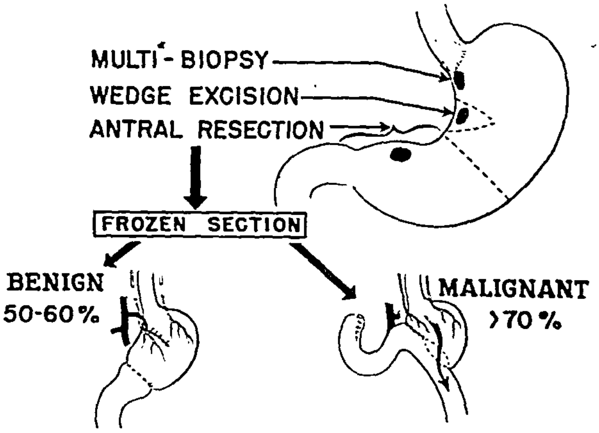

Fig. 1.—Schema of surgical principles employed to avoid radical resection for gastric ulcer. Diagnosis by means of biopsy and immediate frozen section examination allows closure of biopsy site and conservative distal resection, if lesion is benign. Radical resection should be performed only when indicated.

During the past three years radical gastric resection has been avoided unless there was proof of malignancy by frozen section study at the time of surgery (fig. 1). After a general exploration of the abdominal cavity the location of the gastric ulcer is determined. Any local extension or distant metastasis indicating malignancy is eliminated at this time.

The following program has been adapted according to the location of the ulcer. If the ulcer is located high, near the esophageal gastric junction, evidence of malignancy is sought by opening the stomach and taking several biopsy specimens from around the margin. This is a safer procedure than attempting a complete excision at this high level. If the lesion is proved to be benign by frozen section, the gastrotomy is closed and the distal one-half of the stomach is resected. If the lesion is 5 to 10 cm. from the esophageal gastric junction, the ulcer is excised with a rim of adjacent gastric mucosa. If the ulcer is benign, the wedge opening is closed and a distal hemigastrectomy performed. When the wedge specimen has been taken from the lesser curvature at some distance from the esophagus, the level of resection may be carried out at this point. Occasionally the opening in the lesser curvature is closed and more of the greater curvature is retained for the anastomosis. This is feasible in patients with gastric ulcer since marginal ulceration from excessive hydrochloric acid production is not a problem, as it is in patients with duodenal ulcer. A hemigastrectomy is carried out for an ulcer in the distal one-half of the stomach. If malignancy is found on frozen section study of the resected ulcer, a radical removal of 70% or more is performed, including all of the lesser curvature, 1 in. of duodenum, and the greater omentum.

Certain technical considerations are worth mentioning. In patients with high benign lesions it is advantageous to insure extensive mobilization of the stomach. The greater omentum is detached from the transverse colon as well as the splenic flexure. Further mobilization can be obtained by dividing the vagus nerves and the peritoneal attachment of the fundus of the stomach. The spleen is extensively mobilized by careful and complete incision of the splenorenal ligament. As a result, the fundus of the stomach as well as the spleen can easily be mobilized into the wound and held into position by the placement of a folded towel above the spleen. The left gastric artery and vein are often ligated to facilitate the excision of high-lying ulcers. In such high lesions the removal of the xyphoid process or splitting of the sternum, as recommended by Wangensteen,[12] is helpful.

In performing the wedge excision or biopsy, soft intestinal clamps are applied above and below the ulcer as well as across the left gastric artery and vein. This is done in an attempt to avoid contamination, provide hemostasis, and lessen the chance of distant spread of tumor cells, should the lesion prove malignant.

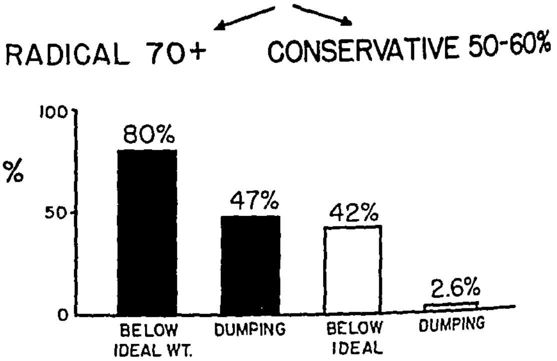

Fig. 2.—Comparison of effects of two types of resection on nutrition and "dumping" symptoms in 76 patients, 38 of whom underwent each type.

If the pathologist finds the ulcer is malignant, it is necessary to remove the lymphatic drainage area of the entire lesser curvature and ligate the left gastric artery at its base. The entire omentum is resected along with 1 in. of the duodenum, depending on the location of the neoplasm. The type of anastomosis constructed depends on the desires of the surgeon. We tend to use the Billroth 1 type; this, in our opinion, is usually technically feasible and will insure a better chance for good postoperative nutrition with fewer postgastrectomy complaints.

Comment

The study of a limited number of cases has supported the use of the more conservative approach to the treatment of a patient with gastric ulcer proved to be benign by frozen section examination (fig. 2). In a series of 76 patients whose progress was followed for more than one year (half of whom had a radical resection and the other half a conservative resection) the difference is apparent. Of those having a radical resection before 1955, 80% were below their ideal weight; about 47%, or almost half, had dumping symptoms of a moderate degree, although only a few were particularly severe and troublesome. In contrast, only 42% of patients treated during the past three years, most of whom have had a more conservative type of resection, were below ideal weight, and the incidence of moderate to severe dumping was relatively insignificant (2.6%).

Perhaps the surgeon has been so gratified with a low operative mortality and disappearance of ulcer symptoms after radical resection for benign lesions that he has overlooked the high incidence of undesirable side-effects. With less radical surgery the mortality is even lower and the chance of recurrent ulcer symptoms is unchanged. While the incidence of recurrent ulceration is relatively low, it has seemed to us that radical gastric resection has had as much adverse effect on a patient with a benign gastric ulcer as a similar procedure has on the patient with duodenal ulcer. In part this may be due to the fact that the percentage of women subjected to gastric resection for gastric ulcer is much higher than that for duodenal ulcer. It is fairly well established that the end-results in gastric surgery for women leave much more to be desired than do those in men.

Although the number of cases is relatively small, we are convinced that investigation of a larger series of patients treated by this conservative approach after the establishment of accurate frozen section diagnosis is warranted. Perhaps, with the improvement in the total end-result of such surgery, more patients with gastric ulcer will be readily recommended for surgical extirpation of their lesion and thereby the opportunity for early removal of small malignancies will be enhanced.

Summary

Because of the relatively high incidence of unsuspected malignancy, surgical consultation is desirable for every patient with gastric ulcer. This physician-surgeon cooperation is just as important as their dual responsibility in the management of massive gastric hemorrhage. More consideration should be given to the role of drugs, gastric irritants, and stimulants in the etiology of gastric ulcer. Perhaps surgery should be delayed until such drugs have been withdrawn and a trial of intensive medical therapy has been carried out.

Routine radical resection for gastric ulcer is not justified just because malignancy occurs in one case out of 10. This is especially true for lesions high on the lesser curvature, where almost total gastrectomy may be carried out for a benign lesion. Several biopsies or wedge excision of the entire ulcer, with frozen section, should precede radical resection. There should be wider application of closure of the gastrotomy wound for high-lying ulcers, and more distal conservative 50% resections should be performed.

From a nutritional point of view, radical resection for gastric ulcer probably does not insure any better results than does resection for duodenal ulcer. However, the incidence of recurrence of marginal ulceration is much lower in patients with gastric ulcer. Better nutrition and fewer disagreeable side-effects will result with frozen section diagnosis and conservative resection. It is hoped that earlier surgery for more patients with unsuspected malignancy will result in improved management of gastric cancer.

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NEWER CONCEPTS OF SCHOOL HEALTH SERVICES

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For the effective care of a school child with either physical or mental handicaps a complete diagnostic picture is essential. It cannot be provided by the parent or the physician or the teacher separately, for each sees different aspects of the child's problem. Various ways of bringing together the necessary information are here described. A school medical adviser can review the available data with the school psychologist and then discuss the findings with the private physician. In communities where there are medical schools, diagnostic evaluation centers can be set up and their findings interpreted to the family by the general practitioner or the pediatrician. In any case, the diversity of health, behavior, and learning problems is such that the school health program must be viewed as a teamwork project with emphasis on the role of private medical practice.

The concepts of school health services treated here have arisen from developments in medicine, public health, and education in a growing suburban county not unlike suburbia elsewhere. We place new emphasis on private medical practice. This has been possible because of progress in health department staff education, which has stressed diagnosis and treatment as essentially the functions of private physicians and not of health departments or schools. This concept is by no means new, but the increase of medical attention received by school-aged children in our community today has prompted us to recognize a new role for the private physician in school health services.

The development of our policies has been shared with our medical society and the school administrative staff so that private practice has been encouraged as a fundamental policy. This has involved the "concept of the school health program as a teamwork project,"[1] which has been demonstrated in an unsurpassed manner by the National Conference on Physicians and Schools, sponsored by the American Medical Association. The teamwork of these national conferences has set a pattern for achieving agreements "despite widely differing backgrounds" of the participants. This has been a challenge for our local application involving several hundred practicing physicians, several thousand school personnel, and nearly 100 health department staff members.

While this paper treats of general concepts, the discussion is largely concerned with handicapped children, because our situation calls for it. The challenge of applying the teamwork approach in Montgomery County has led us to realize the importance of the coordinating function of the health department in its relation to private practice but also to other community resources. Such coordination in our opinion has performed a function that is appropriately governmental only when it cannot be done by people for themselves or by their private physicians.

We show how the need for this coordinating *function is most urgent in connection* with the medical problems of handicapped children who have had or may have private medical attention. We have found that this function also improves the relationship between the health department and the medical society.

We are pleased to note that our policies are consistent with those stated in "School Health Services,"[2] a report published in 1953 and at that time the last word as a "guide for health procedures in small or large school systems." We shall discuss the school medical adviser as an essential means for carrying out the coordinating function with a new emphasis over the report of 1953.

Recent Changes

Medicine.—The benefits from our newer knowledge in medicine have probably had no greater impact anywhere than on the children in these newer communities. Pediatricians and general practitioners both have been in great demand for advice and health supervision. Preventive medicine has never been more effective, and so the advice of the private practitioner has been in demand not only for illness and prevention but also for the child with developmental anomalies, learning difficulties, and emotional disturbances.[3]

Public Health Practice.—Public health practice in new communities has been generally effective in communicable disease control. Individual housing, sanitation, and environmental problems are minimal compared with other problems. As health depart-

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ments, medical societies, and the voluntary health agencies with specialty interests have discovered how much they have in common, public health practice is becoming more and more concerned with problems of mental health, chronic disease, rehabilitation, and diagnosis. This is the field of public health practice which requires community organization and action today. In that sense it is like the social action that was necessary to prevent epidemic disease such as typhoid and diphtheria at the turn of the century.

The neglect of diagnosis, treatment, and rehabilitation for chronic disease, mental illness, and mental deficiency is today as surely the business of public health as neglect of epidemic disease was 40 years ago. We must be concerned not only for humanitarian reasons but also because this burden falls on all of us.[4] We know full well that there is a breaking point beyond which the stress and strain of chronic disease, mental illness, mental deficiency, disability, crippling handicaps, misery, and hopelessness cannot be endured. We are challenged by this broad social problem and the role that medicine, public health, and education can play through teamwork.

Medicine and public health practice have made a splendid beginning for the relief and prevention of these conditions in children. There are many encouraging signs for prevention on all fronts. Some conditions can be cured; many can be compensated; most of them can be alleviated. When the trusted family physician, auxiliary medical services, and public health and school personnel can pull together, family and loved ones can always be comforted. This teamwork improves the prospect of all benefits. It is this pulling together on health problems which is particularly the role of public health practice. Only through cooperation and unified policy can medical practice and education make the proper use of all the medical and social resources which are essential for the relief and prevention of these causes of misery and inadequacy.

Education.—Recent changes in education have not been limited to keeping up with the growth of the school population. The schools are indeed catching up with the concept of the White House Conference of 1930, which emphasized the rights of crippled children to an equality of opportunity. Schools are recognizing the true economy of education and physical care for the handicapped to produce self-supporting and useful citizens and are beginning to alleviate the burden on society of handicapped children who will always need a protecting environment.

Many forces are contributing to this enlightened interest in the handicapped and otherwise exceptional child. Not the least of these forces have been the courageous parents of cerebral palsied and mentally retarded children. They have dared to face the world as parents of children with limited gifts, and they have organized to challenge our apathy and shortsightedness in excluding these atypical ones from public schools. Social and psychological researches have contributed new concepts concerning individual differences so that we no longer look on slow learning, mental deficiency, and various handicapping conditions in terms of heredity. There is even some evidence of the growth of the idea that individual persons have the right to develop their inborn potentialities.

For many years the idea of education for all the children has gradually been contributing to a broader interest in the education of handicapped children. This has led to many demonstrations of special education methods. Carefully selected and dedicated teachers have helped to build up evidence indicating that many types of exceptional children can benefit from special education. Children who are restless, overactive, and highly distractible usually interfere with the learning of other children; yet the skilled teacher with a small enough class can provide a structured situation so that learning can take place.[5] To be managed effectively aggressive children who are emotionally disturbed may also require special teaching skills and small groups.

Whenever the child who interferes with the learning of other children has been removed from a regular class, the improved opportunity for normal children has been so obvious that those who see the improved learning immediately recognize the value of special education. Principals and teachers thus recognize how special education benefits both the children in regular classes and the children who are handicapped. This idea has spread so that it is beginning to play a part in the remarkable advance in special education.

New Demands and New Opportunities

The major public health problems of school-aged children in new suburban communities are no longer the control of communicable diseases and the finding and correcting of physical defects.[6] We still have these problems with us, but they no longer require a major portion of the time of public health nurses and school physicians. Where many children have health supervision through private medical practice, only occasionally is it necessary for public health nurses and school physicians to do things to and for children. We now have an opportunity to tackle, through school health services, some of the problems that may lead otherwise to the breakdown of families, nonproductive citizens, dependency, delinquency, and the problems of children who are already a drag on the regular classes in school.

Both private practitioners and educators are facing more and more demands for advice concerning handicapped and emotionally disturbed children. As educators place more children in special classes, they gain a clearer focus on atypical children, revealing many with symptoms strongly suggestive of the need for special studies and medical advice. The high cost of special education gives the educator particular concern for the placement of the right children in appropriate special classes. Almost invariably special education supervisors and teachers recognize atypical children who need careful diagnostic studies.

From the educator's standpoint, the answer to this problem of diagnostic studies is usually a referral of all children to a polyclinic or diagnostic center whenever the parents cannot produce an impressive medical report. Educators are usually not aware of the fact that a pediatrician is the coordinator of the medical specialties for children in any diagnostic center nor of the extent of the medical study which may have already been given by the private physician. On the other hand the physician may not be aware of symptoms and behavior observed by the teacher which influence the child's ability to receive an education and the school's ability to educate him. School health services can bring closer understanding to the interpretation of medical and educational viewpoints for the child in question. This important concept will be amplified in the following paragraphs.

From the public health administrator's standpoint the problem is not so much to provide services for handicapped and disturbed children as to see that the community has a mechanism by which physicians and parents are able to use effectively the medical resources of the community. This function of coordination of activities and resources was described in an official statement of the American Public Health Association adopted Nov. 1, 1950.[7] We would add that it is a responsibility of both the public health administrator and organized medicine to take the lead in the development of medical resources when qualified medical, auxiliary, and hospital facilities already established cannot meet children's needs.

Today's Problems

We have pointed out how changes in medical practice have come from advances in preventive medicine, regular child-health supervision, and an ever-increasing proportion of the school-child population being served by a closer doctor-parent-child relationship. From both parents and physicians in recent years we have noted that more parents discuss their child's school problems with their private physicians, and our impression is that this is the result of the gain in child care that has come from more health supervision and closer doctor-parent-child relationships.

As private physicians have called on us to find out how their young patients were getting along in school, we have recognized how difficult it is for the private physician to learn what the school staff have observed about their patients and what they can do for them.

Ordinarily, in office practice the private physician can learn what goes on in school only from the parent and the child. For the child above primary age the skilled physician may, of course, learn much of what is disturbing the child by an indirect approach to the youngster. But parents find it difficult to be objective about their own child. Rarely are they able to evaluate the teacher's competence. The standardized group test results are not well understood by the parent. Even when the school has considerable objective data from the school psychologist, the parent cannot give a reliable report.

The chances are that school personnel do not appreciate the medical aspects of children's problems. Neither do they understand the potentialities of the doctor-parent-child relationship and how much it may contribute to a wise decision for a definitive consultation or effective treatment. They may even recommend with all the authority of the school system that a parent seek a particular kind of specialist. Just as frequently they assume that they can deal with a problem because they believe they can recognize a situation calling for medical help. School personnel often do not know when a child is under treatment or whether the private physician has the background information that is essential to understand the child's behavior.

As we have seen how confused some parents and teachers have become when they encounter different advice from physicians and educators, we have come to the conclusion that coordination between medicine and education is a major problem. Most children with emotional and learning problems are not studied by child psychiatrists. We are not convinced that it is necessary. At any rate, at this stage of our knowledge, physicians and educators need to be aware of problems such as Dr. Lauretta Bender[8] mentions in her studies, e. g., "an educational problem in children variously designated as learning disability (including reading, spelling, and writing disability), language retardation, developmental or maturational alexia, dyslexia, dyslalia, or aphasia, word deafness and word blindness, or cortical deafness and blindness." When these conditions are a part of the picture, it is particularly important that educators and physicians give advice with some agreement.

School Medical Adviser

For children with multiple handicaps and particularly anxious and confused parents, we have noted how often educators and private physicians try to coordinate their advice to parents. However, they usually fail to get together because it is just too difficult. To deal with this lack of communication we have employed pediatricians on a session basis to go to schools by appointment and consult with the interested school personnel. Such school medical advisers can understand the viewpoints of both educators and private physicians. They can benefit from the observations of the child in school and can interpret the school situation to the private physician. Reports from the school psychologist are particularly valuable when the school medical adviser can review the data first hand with the psychologist and then discuss the findings with the private physician.

The role of the school medical adviser is equally important to the school personnel when the insight and knowledge of the private physician is brought back to the school and interpreted by the pediatrician. With this liaison we can also insure the proper use of medical resources for diagnosis, treatment, and counseling of parents.

The challenging character of the complex problems of handicapped children is sufficiently interesting for well-qualified pediatricians to be interested in this service. The interchange of information with school and medical observers provides experience contributing to an understanding of the mental health of children. With good nurse-teacher rapport the nurse has an opportunity to learn which children have learning and behavioral problems. If she is well qualified with knowledge of growth and development and child psychology, she can interpret to school personnel the value of the medical point of view. On the other hand, public health nurses may need the encouragement and support of competent supervision in order that the school principal and the personnel worker among the pupils may recognize these values. In our experience it is not enough merely to offer a channel of communication between education and medicine. It must be demonstrated.

One of the best opportunities for demonstrating the value of communicating with the private physician and the contribution of the pediatric adviser is when the child is being considered for placement in the special class. Up to this point it is difficult for school personnel to appreciate the role played by the private physician in planning with the parent for diagnostic studies, therapy, or counseling. Until demonstrated there is little awareness of the parents' confidence in the private physician or the significance of the doctor-patient relationship gained through services in sickness and in health.

The value of a doctor-to-doctor telephone discussion of the child's problems is well demonstrated when the private physician has already been working on the problem. For example, the important role of the private physician is obvious when school personnel learn that the child's behavior can be understood in terms of significant social and family history known to the private physician, that the child is under treatment for a convulsive disorder, that psychological studies have already been recommended by the private physician, or that psychiatric help has been prescribed. When school personnel think a particular kind of medical specialist is needed to help them understand the child, the pediatric adviser in the school can make clear the value of communicating with the private physician by interpreting the special studies already made, by explaining the diagnostic steps that are indicated, and by arranging for such diagnostic service with the private physician.

Such demonstrations for prospective special-class children can bring about a realistic integrative approach to the dynamics of growth so that school, parents, and private physician can work together in the interests of the child. Demonstrations for special-class children open the door to the school medical adviser to be invited to the school for children with less severe handicaps.

We have noticed there is a great deal of discussion in both educational and pediatric circles about the interdisciplinary approach to problems of learning and behavior of children. While there is awareness of the problem, we have not been able to see how it can be met without a pediatric adviser as liaison. The turnover of professional staff in the schools and among public health nurses is sufficient to require continued staff education and demonstrations to achieve teamwork involving both medical and educational judgment. In fact, the professions of medicine and of education both have strong traditions for cooperation within their own groups, but they unconsciously tend to extend their own qualifications—from medicine to education and from education to medicine. As James Harvey Robinson said, "Men are ordinarily peaceful within their group, or at least do not exhibit their individual pugnacity in any deadly form; but let the ancient, inherited group spirit be aroused, and the most highly cultivated men will rush to arms. . . ."

Diagnostic Evaluation Centers

Most communities that have faced up to the high prevalence of physical, mental, and emotional handicaps have set up diagnostic facilities to avoid neglect of children when cost may interfere with the diagnostic studies. For those communities with a medical school, the diagnostic evaluation center generally provides facilities for professional medical training as well as services for handicapped children.[9] However, a diagnostic evaluation center or a group of clinics in a hospital is not the only way to achieve cooperation among medical specialists. The general practitioner or the pediatrician, who knows the family and who is the trusted medical adviser, can coordinate and interpret the findings of the specialists.

Whether there is a well-organized university medical center with an interdisciplinary diagnostic clinic set-up or whether all the studies are done by private specialists, on referral, with the coordination by the private pediatrician or family physician, there is still need for coordination of medical judgment with the educator's judgment if we are to consider all the disciplines that are involved in understanding the child. For the more complex problem of those with multiple handicaps, men of both medicine and education should have an opportunity to give their interpretation of the child's abilities, disabilities, and functional development as well as his dysfunctions. The concomitant handicaps which result from his primary handicaps should be interpreted from both the medical and the educational standpoints. Thus, a motor defect may interfere with the development of his mental potentialities, or a speech difficulty may delay his social adjustment.

We have emphasized the difficulties of medicine and education, both of which attempt to consider separately the same facts about a single child. We cannot bridge this gap between the two professions without joint planning to achieve an acceptance of the principle that both professions are needed to place the right children in appropriate special classes. In our experience the school medical adviser can bridge this gap.

Summary

In the application of the "concept of the school health program as a teamwork project" in a new suburban county of generally high economic status, emphasis has been placed on the role of private medical practice. Changes in medicine, public health practice, and education relating to school health services and the coordinating function of the health department have called for more attention to children with such handicaps as learning disabilities, mental deficiency, emotional disturbances, epilepsy, defects of speech and hearing, cerebral palsy, and other crippling conditions. Experience with these problems has indicated the limitations of educational planning for such children when there is no satisfactory liaison with the medical profession. The work of part-time pediatricians as medical advisors can bridge the gap between medicine and education.

Box 471 (Dr. Peeples).

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HYPNOSIS IN PAINFUL TERMINAL ILLNESS.—Hypnosis is a state of intensified attention and receptiveness and an increased responsiveness to an idea or to a set of ideas. There is nothing magical or mystical about it. . . . Normal everyday capacity for intensely directed attention can be employed to concentrate and redirect a patient's attentiveness and responsiveness in an altered fashion so that he benefits through a new and learned responsiveness to selected stimuli. This constitutes the use of hypnosis in painful terminal disease. . . . Three case reports indicate definitely that hypnosis can be of value in treating terminal painful illness. However, it is not to be regarded as an absolute answer to all the medical problems involved. Rather, it is one of the possible approaches in the handling of the patient's problems that possesses special and highly significant values at both psychological and physiological levels. While hypnosis can sometimes be used alone as a means of pain control in carcinomatous disease, more often it is properly used as an adjuvant. In that capacity it can serve to diminish significantly the actual drug dosage and to effect a much greater relief both mentally and physically. In all probability, the more comprehensive psychologically the hypnotic approach, the greater is the possibility of therapeutic results.—M. H. Erickson, M.D., Hypnosis in Painful Terminal Illness, *The Journal of the Arkansas Medical Society,* July, 1959.

HORIZONS IN PATHOLOGY

Thomas M. Peery, M.D., Washington, D. C.

The history of the Section on Pathology and Physiology reveals changes of name and shifts of emphasis that reflect the developments in both sciences since 1859. The recognition of pathology as a specialty followed the development of microscopy, and the formal training of specialists in pathology began in 1886. The rapid developments of the past 50 years justify certain predictions as to the future. Laboratory tests, largely mechanized to increase accuracy and facilitate handling of results, will be adapted to extensive screening programs. Pathology, while maintaining its status as a basic science, will emphasize its application to patients in hospitals, and medical students will be more regularly assigned to clerkships in clinical pathology before beginning their regular ward service.

We celebrate this year the 100th anniversary of the Section on Pathology and Physiology of the Scientific Assembly of the American Medical Association. Six other Sections are also observing their centennials in 1959.

The line of descent of our Section begins with the Section on Anatomy and Physiology, which was one of the four sections originally proposed in 1859.[1] A continuity of sorts has been maintained by joining the word Physiology to the title of first one and then another section of the Assembly. In sequence the title changes of the Section were as follows[1]: Medical Jurisprudence, Physiology and Hygiene (1865); Practical Medicine, Materia Medica and Physiology (1873); Practical Medicine and Physiology (1890); and Physiology and Dietetics (1891). This section was subsequently joined with the Section on Pathology and Bacteriology, which had been organized in 1900, to form the Section on Pathology and Physiology (1901).

For its first few years the Section on Pathology and Physiology was intimately related to the scientific exhibits of the Annual Meeting. Both the organization of the Section and development of exhibits were proposed by Dr. W. W. Keen, the noted Philadelphia surgeon, in his presidential address before the Association in 1900.[2] Dr. Keen appointed two committees, one for each purpose, with Dr. Frank B. Wynn of Indianapolis as secretary of both committees. Dr. Wynn was undoubtedly chosen for this double honor because he had been successful in forming an exhibit for the annual meetings of the Indiana State Medical Society. In 1897 this exhibit consisted of pathological specimens contributed by the members of the state society.[3] Repeating his appeal in subsequent years, Dr. Wynn had accumulated some 800 specimens by 1899. The Indiana Society was so enthusiastic in its endorsement of this teaching display that it appropriated $300 to ship the exhibit to Columbus, Ohio, where the Annual Meeting of the American Medical Association was held in 1899, one month after the exhibit had been shown at the state meeting. This was the only purely scientific exhibit at the meeting in Columbus, and as such it attracted a great deal of enthusiastic attention.

This pathological exhibit was the beginning of the Scientific Exhibit, which is such an outstanding feature of the Annual Meetings of the American Medical Association. Dr. Wynn served as Director of the Scientific Exhibit until 1916 and expanded its scope to include all of medicine rather than pathology alone.[4]

I have traced briefly the history of our Section since its founding 100 years ago. Now I shall review the development of the science of pathology in America, to provide perspective for a look into the future.

Development of Pathology in America

One hundred years ago "pathology" was the hobby of many American physicians and surgeons who collected and preserved specimens as tangible evidence of their enthusiasm for science. In particular the teachers of medicine in these early times prided themselves on their specimens and used them to make their lectures more vivid and understandable. These specimens were the visual aids for teaching medicine in that era. Thus we have the formation and growth of pathological museums in American medical schools, patterned after those in Germany and England.

Note that so far I have referred to pathology and have not spoken of the pathologist. This is because in those early years pathology both here and abroad was "the practical concern of all progressively minded physicians and surgeons" rather than the domain of a specialist.[5] It was a side line, not a field of practice. In our medical schools the chairs of pathology were usually occupied by practicing

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From the Department of Pathology, the George Washington University School of Medicine, and the George Washington University Hospital.

Chairman's address, read before the Section on Pathology and Physiology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 11, 1959.

in micro[illegible] before one could exp[illegible] it was necessary that he become proficient in the technical skills required for the use of the microscope itself. The preparation of thin transparent sections for staining and examination required a knowledge of the practical chemistry of fixatives, dehydrating agents, solvents, mordants, and dyes. Even after these skills had been learned, one had to acquire sufficient experience to make valid observations, to distinguish fact from artifact. All of this required time and special training and made pathology a vocation instead of a hobby. The pathologist appeared as a specialist, and the microscope marked his crest.

Prior to 1886 there was no opportunity for the training of specialists in pathology in the United States. There was no one here competent to teach the subject, and there were no facilities for instruction in the field. In 1886, after several years' study in Europe under some of the most noted teachers of his time, Dr. William H. Welch, at the Johns Hopkins Hospital and Medical School, offered the first course in America for the practical instruction of physicians in pathology and bacteriology.[6] From Dr. Welch's laboratory at Johns Hopkins came the first American trained pathologists, and from them in turn has sprung the specialty of pathology as we know it in the United States today.

Clinical Traditions of American Pathology

Welch emphasized the importance of a close relationship between the pathologist and the clinician and insisted that the department of pathology be located in the closest possible proximity to the hospital wards.[7] Nevertheless, pathology developed for a number of years along the lines of the other basic sciences in the medical schools rather than as a clinical science in the hospital. Undoubtedly this orientation toward research was necessary before the new science could have clinical application.

Today it is generally recognized that pathology is both a basic science and an important clinical specialty for service to the patient. As a clinical specialist, the pathologist provides definitive answers to specific questions regarding a patient's illness. Does this patient have diabetes? Will this patient's anemia respond to iron therapy? Is this patient's breast lump cancer? When the pathologist provides the answers to questions such as these in the care of individual patients, he is functioning as a clinical practice; without this source of new ideas and this testing place for old ideas the dimensions of our specialty tend to become shallow and narrow.

Ever-Widening Scope of Clinical Pathology

The field of pathology has grown rapidly in the last 50 years as a result of the clinical application of fundamental research. We should always remember the debt our specialty owes to the research workers in the other basic sciences. As Davidsohn[8] has noted, it is in clinical pathology that "yesterday's research becomes today's routine."

It is my opinion that the scope of clinical pathology will continue to expand indefinitely. Whereas some specialties, notably syphilology, have experienced a shrinkage of their fields as a result of the contributions of research, the opposite is our prospect. From my own experience I would estimate that the number of laboratory tests performed in relation to a given number of hospital beds has increased by about 50% in each of the last two 10-year periods. Part of this increase is due to the shorter patient stay and the resultant greater proportion of acutely ill patients within a given bed capacity. Even more, however, is the increase due to the fact that the up-to-date clinical pathology laboratory has more to offer, both in the variety of tests and in their dependability, than did its counterpart 10 years previously.

This rapid expansion of services accounts for most of the pressing problems which confront the clinical pathologist today. First and foremost, we find that no one pathologist can possibly encompass all that must be known for the proper expansion and development of laboratory services. A hospital that required only one pathologist 10 years ago now needs two. The answer, I think, is in the group practice of clinical pathology, each member of the group bringing certain special qualifications and interests to supplement those of the other members of the group.

Second, there is a perpetual shortage of those skilled laboratory workers who are so necessary for the expansion and diversification of our services. Certainly we must look in a number of different directions for the answer to this problem. We must recruit and train increasing numbers of highly skilled, professional medical technologists, and we must see to it that they are well compensated. They must work at the highest level of which they are capable, leaving the less skilled tasks for those less qualified. In order to avoid an increase in costs, we must increase the productiveness of our staff by making full use of automatic and mechanical equipment.

Third, there is the widespread problem of crowding in the laboratory. Probably no other division of the hospital outgrows its space allotment as quickly as the department of pathology. The increased number and variety of tests necessitate a larger staff and more equipment; extra bench and office space are needed to accommodate them. In new hospitals space should be provided over and above estimated immediate needs so that pathology laboratories will not already be inadequate before the assigned space is occupied, as is often the case now.

Anticipated Changes in Clinical Pathology

I predict that the next 10 years will see a tremendous increase in the use of laboratory tests for the screening of presumably healthy persons. Such tests, used thoughtfully to supplement the standard physical examination, can be very effective in revealing potential sources of trouble in well patients. The physical examination alone is not sufficient; chest x-rays, blood cell counts, serologic tests for syphilis, urinalyses, and cytological examinations have probably identified more instances of serious disease in supposedly healthy persons than have physical examinations. The specific tests to be used should be determined by careful consideration of a number of factors, including age, sex, occupation, and family history. If any of the tests yields an abnormal result, careful clinical examination and evaluation should lead to the correct diagnosis and provide the basis for successful treatment. Screening tests should be based on automatism wherever possible so as to keep unit costs low while permitting a great increase in the number of tests.

Cytological methods will almost certainly find greater use in the future, and I believe that the biopsy will continue to increase in popularity. Its use in the study of minute bits of tissue obtained by needle puncture will probably increase, whether we as pathologists approve or not.

If the methods for determination of the ketosteroid levels can be simplified, it is likely that they will find a greatly increased use in problems of growth and development, infertility, hypertension, and other "metabolic" disorders.

Automatic equipment will probably revolutionize the practice of clinical pathology. There are now available certain new basic scientific instruments which by adaptation and combination, as in the "AutoAnalyzer," promise an even greater degree of automation than is currently available. Thus a proportioning pump could be joined with a continuous-flow recording colorimeter to increase the speed and accuracy of our hemoglobin level determinations. Modification of Coulter's electronic particle counter might permit its operation as a continuous-flow device in conjunction with an automatic sampler plate and a proportioning pump and thereby make the enumeration of leukocytes and erythrocytes an almost totally automatic process. It even seems possible that the differential blood cell count could be made automatic by the use of fluorescent stains and a television-type scanner, as has been proposed for the screening of cytology smears.

Mechanization will probably permit the clinical pathologist to achieve a degree of accuracy that was previously possible only when tests were performed in triplicate. When that time comes, we can anticipate that our colleagues in clinical research will ask us to perform their tests. They will ask us because potentially we can offer better service than they can develop, and at a much lower cost.

In the small research laboratory everything is in triplicate, especially the costs and the headaches! After the investigator has received his grant, he generally spends at least a month searching for a qualified technical assistant. With her help he then orders the equipment for the laboratory, duplicating several expensive items already available in the clinical laboratory. When the equipment arrives, they spend several weeks in setting up the laboratory in space sorely needed by the clinical pathologist. By the time the laboratory is ready, summer has rolled around and the investigator goes on his vacation. When he gets back, the technical assistant takes some time off. Perhaps after four months of the grant period the team is ready to begin work on patients, but by this time the technician is pregnant or has a better job and so the investigator must start all over again. This harrassment is typical but so unnecessary. I believe that the clinical investigator will, in the future, purchase services from the clinical pathologist to the ultimate advantage of all concerned.

Anticipated Developments in the Teaching of Pathology

Although there is in some circles a move to emphasize the basic science aspect of pathology by having students participate in animal experiments, I suspect that the ultimate change in emphasis will be in the opposite direction, i. e., toward the hospital. After the theories and generalizations of anatomy, biochemistry, physiology, and bacteriology, the student is anxious to learn of disease and of sick people. This can best be done by using the gross and microscopic alterations in the organs and tissues to explain the symptoms and physical signs and roentgenographic changes in the individual patient.

After a student has received instruction in pathological anatomy, oriented toward the patient, I would like to see him spend a brief clerkship in physicians or surgeons, and it was not at all uncommon to recognize the accomplishments of the professor of pathology by rewarding him with the chair in medicine or surgery!

The appearance of the pathologist as a specialist can be traced to the development of the microscope as a tool for medical research and clinical investigation. The microscope opened up entirely new vistas in organ structure and function, in microbiology, neoplasia, and other fields. But before one could explore these promising frontiers it was necessary that he become proficient in the technical skills required for the use of the microscope itself. The preparation of thin transparent sections for staining and examination required a knowledge of the practical chemistry of fixatives, dehydrating agents, solvents, mordants, and dyes. Even after these skills had been learned, one had to acquire sufficient experience to make valid observations, to distinguish fact from artifact. All of this required time and special training and made pathology a vocation instead of a hobby. The pathologist appeared as a specialist, and the microscope marked his crest.

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Pathology must always be oriented toward clinical medicine and the hospital. Proficiency in pathology can no more be achieved in the isolation of the medical school or research institute than can surgical judgment be acquired in the experimental surgical laboratory. We need constant reference to the day-to-day routine of the hospital to give breadth and depth to our teaching, research, and practice; without this source of new ideas and this testing place for old ideas the dimensions of our specialty tend to become shallow and narrow.

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After a student has received instruction in pathological anatomy, oriented toward the patient, I would like to see him spend a brief clerkship in clinical pathology before beginning his regular ward clerkship. During this preliminary period of about a month, I would assign him cases embodying common problems of clinical and laboratory diagnosis. I would require him to participate in the diagnostic studies in the bacteriology, chemistry, and hematology laboratories, reporting his observations at scheduled conferences conducted by the clinical pathologist.

At the graduate level, I predict that medical residents will be more regularly assigned for training in clinical pathology. Surgical residents have long been offered periods of study in pathological anatomy, and most of them have derived permanent benefit from the experience.

Research Horizons in Pathology

It is likely that studies in cancer will continue to dominate research in experimental anatomic pathology. The techniques of histochemistry and radioisotopes will undoubtedly be used extensively in probing for the secrets of the cell nucleus.

In the field of hematological research, thrombosis will probably receive much study. It seems likely that there are fundamental differences between thrombosis within a blood vessel and clot formation in a test tube and that new research methods will be needed to explore the former. The relationship of thrombosis to elevation of the blood cholesterol level is suggestive in its implications regarding atherosclerosis. (Which comes first, the thrombus or the plaque?)

Near the horizon, but likely to be upon us before we know it, are chemical tests for the diagnosis of nervous and mental diseases. On the one hand, we know that in some patients severe mental illness may be alleviated by chemical "tranquilizers." On the other hand, a clinical syndrome similar to parkinsonism in some cases and to myotonia in others has been noted to follow the use of the tranquilizers in certain instances. These two observations suggest that some psychotic states and neurological disorders may have an essentially chemical basis. If so, it is likely that chemical tests can be devised to aid in their recognition and treatment.

What lies beyond these horizons it is impossible to say. We do know that we have at hand great potential resources for discovery and achievement and for the relief of human suffering.

May the next 100 years reveal to our successors a continual unfolding of truth.

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NATURE OF STAPHYLOCOCCIC INFECTIONS.—Intracellular residence may protect staphylococci from substances in extracellular fluids which ordinarily destroy them. The studies of Tompsett indicate that intracellular staphylococci are protected from antimicrobial drugs present in the surrounding milieu. From 50 to 200 times the amounts of penicillin or streptomycin necessary to kill extracellular staphylococci are required to appreciably affect intracellular staphylococci. . . . It appears clear that this protection cannot be explained by simple failure of antimicrobials to reach the interior of leukocytes. What seems more probable is that staphylococci are metabolically less active within cells and that this sluggishness conditions their susceptibility to antimicrobial drugs. . . . Intracellular survival may also modify the way staphylococci behave within the vascular system of experimental animals. When large numbers of staphylococci are injected into the rabbit blood stream, the majority of microorganisms are removed during the first 10 to 15 minutes by the liver and spleen. Then something happens abruptly. The splanchnic tissues no longer trap staphylococci, and a prolonged bacteremia lasting for hours, indeed for many days, results. . . . This is not the case with bacteria commonly destroyed within phagocytes. . . . It is our current belief that staphylococci surviving within polymorphonuclear leukocytes may play a role in this surprising persistence of microorganisms within the blood stream.—D. E. Rogers, Observations on the Nature of Staphylococcal Infections, *Bulletin of the New York Academy of Medicine*, January, 1959.

PERFUSION TREATMENT OF PATIENTS WITH CANCER

Oscar J. Creech Jr., M.D., Edward T. Krementz, M.D., Robert F. Ryan, M.D.
Keith Reemtsma, M.D., James L. Elliot, M.D.
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Perfusion techniques in the treatment of patients with cancer consist in circulating solutions of anticancer drugs through the blood vessels. If the neoplasm is limited to a part that can be isolated, regional perfusion is used; if this is not possible, marrow is first removed from the sternum and iliac crests, total-body perfusion is carried out, and the marrow is reinjected intravenously after the perfusion has been completed. Perfusion methods were used in 145 patients with cancers, 72 of which were carcinomas. There were 56 perfusions of the lower extremity. Perfusion made it possible to attain, in the tumor-bearing area, 15 to 20 times the concentrations obtainable by systemic administration. No specificity of an agent for a given tumor was found, and none of the agents tried was curative. The complications of the treatment in most instances were not serious, but there were eight operative deaths. The best results were obtained in patients with malignant melanoma.

Critical appraisal of the treatment of patients with cancer during the past 25 years leads to the distressing conclusion that, for all its variety, therapy is little more effective now than it was a quarter of a century ago. With some exceptions, about the same number of cures were obtained then as now; for the patient with advanced cancer, death is as relentlessly certain now as then. To be sure, better methods of diagnosis and improved supportive care of the surgical patient have resulted in the treatment of an increased number of patients with localized curable tumors and in a lower operative mortality. Still, in terms of the ability to eradicate human cancer, operation and irradiation are little more effective now than they were formerly.

An awareness of the limitations of existing forms of therapy led to investigation of the treatment of cancer patients with chemical agents. Nitrogen mustard was first employed in the treatment of lymphosarcoma in the mouse about 18 years ago,[1] and in the ensuing years an enormous amount of effort has been devoted to finding effective cancericidal drugs. Yet, once again the fact is inescapable that the patient with advanced cancer, exclusive of cancer of the breast and of the prostate, dies just as surely and with about the same severity of symptoms as he did before the era of chemotherapy.

There are two main reasons for the failure of cancer chemotherapy. In the first place, it has been necessary to search for a cure before the cause of cancer could be found. Second, the toxic side-effects of anticancer drugs which have been developed necessitate the use of doses too small to be curative. It appears that the dilemma created by having to look for "cure before cause" will be resolved in the foreseeable future, and specific drug therapy for cancer will emerge. In the meantime efforts to improve the effectiveness of existing chemotherapeutic drugs must be continued. One way of increasing the effectiveness of an agent is to increase its concentration in the tumor-bearing tissues. Klopp and associates[2] attempted to accomplish this by intra-arterial administration of nitrogen mustard and were able to demonstrate an increased tumoricidal effect. However, it was necessary to use relatively small individual doses to avoid arterial and local tissue injury. The depression of hematopoiesis, while a limiting factor, was not as severe as that after intravenous therapy. Recently we have attempted to develop techniques for administering high concentrations of chemotherapeutic agents in such a way that the toxic effect on the marrow is reduced without impairing the cancericidal effect of the agent. These perfusion techniques have been used in the treatment of patients with cancer for the past two years and the results of this experience are reviewed here.

Techniques

Techniques of perfusion have been described in detail elsewhere.[3] In general, they are of two types: regional and total-body. In the former an attempt is made to confine the effects of a chemotherapeutic agent to the tumor-bearing area (fig. 1). This technique is applicable to regionally confined but nonresectable neoplasms and includes methods for perfusing the extremities, pelvis, lung, breast, oropharynx, and brain. Total-body perfusion is the term applied to chemotherapy of disseminated cancers for which regional perfusion would be inappropriate.

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The techniques of regional perfusion vary somewhat, depending on the area to be treated, although the underlying principles are the same. The artery and vein supplying the part or region are occluded proximally, cannulated in a distal direction, and connected to an extracorporeal circuit consisting of arterial and venous pumps and a bubble oxygenator. In perfusing the extremities a tourniquet is applied, proximal to the sites of cannulation, thus effectively, if not completely, isolating the perfused part from the systemic circulation. In the treatment of lesions within the pelvis, tourniquets are applied to the upper part of the thighs and the patient is placed in such a position that the lower half of the body is dependent. Perfusion of the lungs requires the use of two extracorporeal circuits, one for the heart and lungs and one for the systemic circulation. In perfusion of the breast, oropharynx, and brain the chemotherapeutic agent is less well confined to the tumor-bearing area than in perfusion of other areas. When a tumor is confined to the foot or lower portion of the leg, perfusion of the extremity from the knee down is accomplished through the lower superficial femoral artery and vein. For lesions on the thigh, "hindquarter" perfusion is done through the external iliac or common femoral vessels. Similarly, for lesions of the hand and wrist, perfusion of the forearm is carried out, usually through the brachial artery and vein. For lesions about the arm and axilla the axillary vessels just below the clavicle are cannulated; for lesions of the shoulder, the subclavian artery and vein are used. For tumors of the oropharynx perfusion is carried out through the external carotid artery and the facial and external jugular vein of the ipsilateral side, and for lesions of the brain the internal carotid artery and internal jugular vein are used.

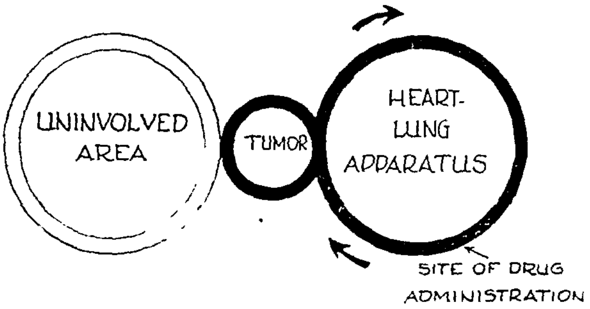

Fig. 1.—Schematic diagram of principle underlying regional perfusion in treatment of human cancer.

Total-body perfusion consists in the removal of marrow from the sternum and iliac crests immediately prior to treatment. Catheters are then passed into the thoracic aorta and inferior vena cava by way of the common femoral artery and vein, respectively, and perfusion is begun. When perfusion is completed the marrow is returned to the patient by intravenous infusion.

Chemotherapeutic Agents

At the beginning of this study, four chemotherapeutic agents were used in the treatment of human cancers. These were the alkylating agents nitrogen mustard (HN_2), phenylalanine mustard (PAM), triethylenemelamine (TEM), and triethylenethiophosphoramide (thio-TEPA or TSPA). Later, actinomycin-D (Act.-D) and 5-fluorouracil (5-FU) became available. Actinomycin-D is an antibiotic that acts primarily on the cytoplasm of the cell, in contrast to the alkylating agents, which are primarily nuclear toxins; 5-fluorouracil is an antimetabolite, producing metabolic block at sites essential to growth of the cell. More recently a combination antimetabolite and alkylating agent (AB 100) has been employed in several cases.

The amounts of these agents that can be administered to various regions depend on several factors, namely, the size of the perfused area, the completeness of isolation, the duration of action of the chemotherapeutic agent, and whether the patient has received prior chemical therapy or irradiation (table 1). For instance, nitrogen mustard and 5-fluorouracil have a short duration of action and may be used in relatively large doses when the perfused part can be isolated. Thus, for the lower extremity, twice the usual systemic dose can be safely administered. In perfusion of the upper extremity, however, the dose of these agents must be reduced because of the small mass of the part. On the other hand, phenylalanine mustard and TSPA remain active for at least several hours. Thus, irrespective of the area perfused, the usual systemic dose should not be exceeded. When an extremity or the pelvis is perfused with these agents, an attempt is made to remove any residual amount of the drug at the end of perfusion by draining the venous system and infusing dextran through the arterial line. Even this maneuver does not entirely eliminate the depressive effects of phenylalanine mustard and TSPA on the hematopoietic system. When chemotherapy or irradiation has been employed in the recent past, the amount of an agent administered by perfusion should be reduced.

Table 1.—*Schedule of Dosage in Milligrams per Kilogram of Body Weight of Five Drugs Used in Perfusion Treatment of Cancer*

	Region				
Agent	Pelvis	Lower Extremity	Upper Extremity	Oropharynx and Brain	Total Body
HN_2	0.8	0.8	0.4	0.2-0.3	0.8-1.2
PAM	1.5	1.5	1.0		
TSPA	1.0	0.8	0.6	0.6-0.8	
Act. D	0.07	0.05	0.035		
5-FU	20.0	20.0	15.0		
AB-100	3.5				

In some instances it may be desirable to combine two or more chemotherapeutic agents. The dose of each will vary, depending on the degree of isolalation of the tumor-bearing area. For perfusion of the extremities, in a case in which isolation is relatively complete, we have used a dose of each agent roughly comparable to that employed when the agent is used alone.

The choice of a chemotherapeutic agent for a given tumor has been largely arbitrary, although based somewhat on our own experience and that of others. In general, phenylalanine mustard and TSPA have been used in the treatment of malignant melanoma and some sarcomas. Nitrogen mustard has been employed in the treatment of rhabdomyosarcoma and carcinoma of the lung, gastrointestinal tract, and breast. TSPA has been used in the treatment of ovarian carcinoma and of neural tumors. Actinomycin-D, 5-fluorouracil, and AB-100 have been used singly or in combination with the alkylating agents in the treatment of adenocarcinoma and some sarcomas.

In administering an anticancer drug several factors must be considered. The available agents, irrespective of their mode of action, are most effective if brought in contact with the neoplastic cell at about the time of mitotic division. Thus, the longer an active agent is in contact with a tumor, the greater the number of cells affected during this vulnerable period. At the same time, the bubble oxygenator becomes less efficient and produces damage to the cellular elements of the blood when it is operated in excess of one and one-half hours. This has limited the length of perfusion. Finally, with perfusion techniques, drug administration is intra-arterial, in that the agent is injected into the arterial line just proximal to the arterial pump. Thus, if a large dose of a vesicant agent such as nitrogen mustard is employed, care must be taken not to administer it in a single injection, since this has been shown experimentally to produce arterial injury and thrombosis.

TABLE 2.—*Summary of Cases of 145 Patients Treated by Perfusion*

Type of Tumor	No. of Cases	No. of Perfusions
Carcinoma	72	74
Melanoma	40	50
Sarcoma	28	33
Glioblastoma	5	5
Total	145	162

Methods of administering chemotherapeutic agents have varied. The total dose of nitrogen mustard or 5-fluorouracil is divided into four or five equal portions, and these are administered three to five minutes apart. PAM and TSPA, having an extended duration of action, may be administered in a single dose or in two equal doses, 10 to 15 minutes apart. When two agents are used in combination, each one is divided into two equal doses and these are given alternately at five-to-eight-minute intervals.

Analysis of Cases

Since June, 1957, 145 patients with cancer have been treated by perfusion methods. The youngest patient was 11 years of age while the oldest was 88, the average age for the entire series being 50 years. There were 69 male and 76 female patients.

Among the 145 patients there were 40 with malignant melanoma, 28 with sarcoma, 72 with carcinoma, and 5 with glial tumors (table 2). Perfusion was performed once in 133 patients, twice in 9 patients, three times in 1, and 2 patients were perfused four times, for a total of 162 perfusions in the entire group. Most of these patients had cancer that was recurrent or metastatic to the extent that cure could not reasonably be expected from any type of therapy, and in these treatment has been classified as palliative. There were 128 in this category. In 17 cases perfusion was carried out as an adjunct to surgical removal of a localized primary tumor.

TABLE 3.—*Summary of Results in 120 Patients Treated by Perfusion*

Tumor	Therapy*	Quiescent	Recurrent After Response	No Effect	Died as Result of†		
					Operation	Chemotherapy	Tumor
Melanoma	A	3	1				
	P	21	6	2	1	2	2
Sarcoma	A	5					
	P	4	10	6			8
Carcinoma	A	6			1		
	P	14	10	22	6		16
Glioblastoma	A						
	P	2					
Totals		55 (46%)	27 (22%)	30 (25%)	8 (7%)	2	27

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* A—adjuvant therapy; P—palliative therapy.

† With exception of operative deaths, patients who died are classified according to response to treatment prior to death.

There were 56 perfusions of the lower extremity, including 6 "hindquarter" perfusions; 22 of the upper extremity, including 7 "forequarter" perfusions; 26 of the pelvis; and 13 of the breast. The lungs were perfused three times, the oropharynx four times, and the brain five times. Total-body perfusion was carried out in 33 cases.

Of the 145 patients, 25 were treated too recently to permit any evaluation of results. Of the remaining 120 there were 33 with malignant melanoma (table 3), and in 4 perfusion was carried out as an adjuvant to surgical excision of the primary lesion. In three of these there has been no reappearance of the tumor after treatment, but in one case recurrence is evident.

There were 29 patients with malignant melanoma who were treated for palliation of recurrent or far-advanced tumors (table 3). Among these, the tumor remained quiescent in 21 and in 6 there was a significant temporary response of the tumor to treatment but the lesions subsequently recurred. In two patients treatment had no effect.

There were five deaths among patients with melanoma, one of which was operative, two of which resulted from widespread metastases, and two of which were due to an excessive dose of phenylalanine mustard.

Among the patients treated for sarcoma, 25 are suitable for evaluation (table 3). In five of these perfusion was done in conjunction with surgical excision of the primary lesion, and in all the disease has remained quiescent. There have been no deaths in this group. Twenty patients with sarcoma were given palliative treatment and among this group there are four in whom the tumor appears to be quiescent. There were 10 patients in whom the tumor showed temporary regression, while 6 patients failed to show any improvement. Eight patients died after treatment, all as a result of their disease.

Of the patients with carcinoma, perfusion was performed in conjunction with surgical excision of the primary lesion in seven, and six of these patients have remained well (table 3). In the 53 cases in which treatment was palliative, 14 patients have shown a significant response in that the tumor appears to be quiescent. In 10 patients an immediate regression of the tumor occurred but there was subsequent recurrence, and in 22 perfusion apparently had no effect on the growth of the neoplasm.

There have been 23 deaths among patients with carcinoma, 7 of which were operative (table 3). Among these was one patient with recurrent metastatic ovarian carcinoma in whom pelvic perfusion was performed in spite of the presence of an anti-e factor that prevented satisfactory crossmatching with blood donors. This patient developed hemolytic anemia as a result of the blood dyscrasia, not of the chemotherapeutic agent, and died on the 10th day after operation. There were two patients with carcinoma of the lung who died soon after perfusion. In one, death was due to necrosis of a large cerebral metastasis, with cerebral edema, and in the other it was due to hemorrhage from the operative site. Of the 23 patients who died, 16 left the hospital after treatment but died from their disease.

Perfusion was carried out in five patients with glioblastoma multiforme, but three were treated too recently to be included in evaluation of results (table 3). In all of these craniotomy and decompression had been performed previously. Four of these patients are alive and improved after treatment and one died of the disease after a period of slight clinical improvement.

In summary, of 120 patients treated by perfusion 55 (46%) have shown significant improvement, in that the cancer appears to be quiescent. In 27 (22%), temporary regression of the tumor occurred but this was followed by recurrent growth. Thirty patients (25%) showed no response to treatment. There have been 36 deaths, 8 of which were operative. Two patients died with severe marrow depression; one of these deaths occurred in the late postoperative period and is classified as both an operative and a chemotherapeutic fatality. The remaining 27 died of their disease.

Complications

Complications of the perfusion treatment of human cancer have resulted from the surgical procedure itself and from the chemotherapeutic agents. The commonest surgical complication has been edema of the involved extremity. A majority of patients who have been treated for tumors of the extremities have had prior regional node dissection which was followed by moderate swelling of the limb. After perfusion edema of the extremity has increased immediately, but the limb has returned to its preperfusion size in two to three weeks. In a case in which regional node dissection has been accomplished in conjunction with perfusion, delayed healing of the skin flaps has been observed, but it is questionable whether this poor wound healing differs in any way from that often encountered after node dissection.

Since a major vein is cannulated and subsequently repaired, venous thrombosis is a potential complication in every instance. However, in this series it has been encountered only twice and in one of these cases thrombosis of the common femoral vein had been present prior to perfusion. At operation thrombectomy was performed, perfusion was carried out, and the vein was reconstituted. Subsequently venous thrombosis recurred and was followed by pulmonary infarction. In another case, perfusion of the upper extremity was followed by axillary vein thrombosis and massive edema of the extremity. In 12 patients in whom a second, third, or fourth perfusion has been performed, thrombosis of the vein has not been encountered in a single instance, nor has arterial thrombosis been a problem. In no instance has there been any difficulty in restoring arterial continuity and peripheral pulses distal to the site of arterial cannulation.

Complications resulting from administration of the chemical agents have consisted in damage to soft tissues of the perfused area, depression of hematopoiesis, and absorption of toxic products from massive destruction of neoplastic tissue. Injury to normal soft tissue is manifested primarily by erythema of the skin over the perfused region. This gradually changes to a brown discoloration which persists for several weeks. These changes are similar in many respects to those observed after irradiation. In some instances edema of skeletal muscle has been observed and is accompanied by moderate to severe tenderness in the involved muscle groups. In the lower extremity, the gastrocnemius muscle is most often affected. This involvement usually runs its course in about three to four weeks. These changes are most severe after perfusion of an extremity and are usually controlled with elastic compression bandages and elevation of the part. When the skin and muscle changes are moderately severe, administration of prednisolone has been effective in relieving these symptoms.

Peripheral nerve injury has been observed after perfusion of the upper extremity in two cases. In one of these the median nerve was involved while in the other there was radial nerve palsy. It is not clear whether nerve injury resulted from the chemotherapeutic agent or from the tourniquet. In both cases there has been a gradual return of function.

Interference with hematopoiesis is manifested by a reduction in the leukocyte and platelet counts (fig. 2). These usually appear about five to seven days after perfusion and persist for four to five days, when recovery begins. In many instances a significant reduction in erythrocyte content has been observed also. This becomes apparent one or two days after perfusion and is probably due to hemolysis, although evidence for this is not always present. In one case a large dose of nitrogen mustard was used for pelvic perfusion and severe hemolysis occurred within 48 hours, evidenced by a significant reduction in the erythrocyte count and elevation of the serum bilirubin content. Hematopoietic changes are observed whenever regional confinement of the agent is inadequate, and their severity depends on the amount of agent used. In most instances leukocyte depression has been mild, although in 19% of cases the leukocyte count has dropped below 1,000 cells per cubic millimeter. In spite of their severity these changes usually respond to transfusions of fresh whole blood, steroid therapy, and administration of antibiotics. In three instances drug-induced leukopenia led to the patient's death.

Comment

This experience in treating 145 patients with cancer with chemotherapeutic agents administered by perfusion has made possible certain observations which appear to be pertinent to the therapy of tumors in human beings. First, and perhaps most important, is the conclusion that under conditions imposed by these methods, none of the anticancer drugs presently available is curative. Although it is possible, by regional perfusion, to achieve concentrations of a chemotherapeutic agent in a tumor-bearing area 15 to 20 times those obtained with systemic administration, in no instance has the response to a neoplasm been indicative of true specificity. To be sure, striking resolution of malignant lesions has occurred after treatment, but in no instance has this response matched that observed, for example, when a hemolytic streptococcic infection is treated with penicillin. It must be admitted that, by the methods described here, a chemotherapeutic agent in high concentration is in contact with the neoplasm for a relatively short time. This is probably inadequate for its maximum effects to be realized. Experiments to develop methods for significantly prolonging the period of perfusion are now in progress.

It is also evident from this study that there is little specificity of an agent for a given tumor. Thus, phenylalanine mustard may produce rapid resolution of metastatic melanoma in one case while in another there will be no response whatsoever, or two or three agents may be employed in successive perfusions before an effective one is found. For example, a patient with subcutaneous metastatic melanoma of the lower extremity was treated by perfusion on one occasion with phenylalanine mustard and subsequently with a combination of phenylalanine mustard and TSPA. There was little response of the lesions to these agents and within a short time they began to grow rapidly. Finally, perfusion with nitrogen mustard was carried out and an interesting and gratifying phenomenon ensued. Within three or four days the skin over the subcutaneous lesions became red and edematous, and within two or three weeks each metastasis, with its overlying skin, became necrotic and sloughed. In contrast, in the first patient treated for melanoma by perfusion with phenylalanine mustard, the lesions began to regress within a few weeks and eventually disappeared.

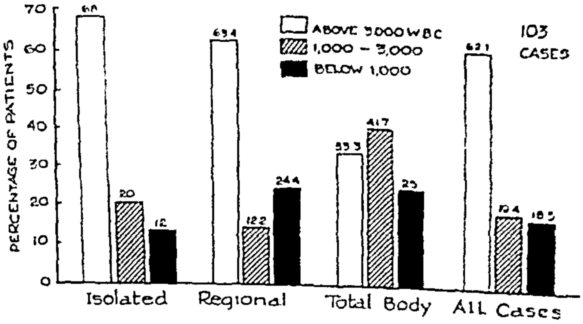

Fig. 2.—Leukocyte depression after perfusion.

Depression of hematopoiesis after perfusion with a long-acting agent is a complication of considerable importance. For instance, a significant leukopenia developed after limb perfusion with phenylalanine mustard and TSPA in about 10% of patients, although most of the agent was confined to the perfused area and attempts were made to remove residual amounts of the agent at the end of treatment. This implies that some of the drug remains in the tissues until isolation of the part is ended, when systemic distribution and marrow injury occur. In addition, it has been suggested recently that absorption of the products of drug-induced tumor necrosis may have a depressive effect on hematopoiesis.[1] In any event, cancer chemotherapy by perfusion requires the same judicious use of an agent as does systemic administration.

As indicated earlier, the initial choice of an agent is somewhat arbitrary. Obviously, a "sensitivity test" is sorely needed. We are now using a test which depends on vital stains to determine the viability of neoplastic cells after their exposure to chemotherapeutic agents, and, while this method has been used in the selection of an agent in about 15 cases, there is no evidence that it is specific.

Certain factors related to perfusion itself are of importance to successful treatment. There are some indications that the tissue should be maintained at or near normal temperature for maximum effectiveness of the cancericidal drug. When an oxygenator is used the temperature of the blood is reduced as much as 10 to 12 F (5.5 to 6.6 C), and this in turn results in significant reduction of temperature of the perfused part. Apparently the decrease in metabolism resulting from cooling interferes with the cytotoxic effect of the chemotherapeutic agent. Thus, measures should be taken to prevent this drop in temperature. In fact, we are now exploring the effects of high temperature on the action of cancericidal drugs.

A second factor of importance is that of pressure and flow in the tumor-bearing area during perfusion. At high rates of flow there appears to be patchy distribution of the perfusate, and at pressures in excess of the systemic systolic pressure, leakage from the perfusion circuit becomes excessive. Therefore, it is desirable to measure blood flow and pressure continuously during perfusion.

The changes which occur in a malignant neoplasm after treatment with a cancericidal agent administered by perfusion are varied and have been studied best in patients with melanoma. Metastases of malignant melanoma show several types of response. Subcutaneous lesions and metastases to regional nodes usually begin to decrease in size within three to four days after treatment and may disappear completely. Less often an intense, inflammatory reaction develops about the subcutaneous nodule and involves the overlying skin. In a patient mentioned earlier these areas sloughed completely.

Cutaneous melanoma usually responds in one of two ways. Small lesions, whether melanotic or amelanotic, become black, flattened, and dried. Often these tumors disappear entirely, leaving a residual freckle. Large cutaneous metastases become hemorrhagic within two to three days after perfusion and go on to ulceration and perhaps to complete disappearance.

Bulky metastatic melanoma may become reduced in size, as a result of tumor necrosis, after perfusion. This seems to produce a peripheral retraction of the tumor so that its involvement of adjacent tissues is diminished. Similar regressive changes have been observed in patients with all of the types of cancer treated. In those with certain sarcomas temporary reduction in size has been particularly striking.

The mechanisms for development of these changes, particularly those observed to occur in patients with melanoma, require further investigation. Certainly, in some instances, it appears that the host-tumor relationship is disturbed sufficiently so that resistance factors gain control of the neoplasm. In some the neoplastic cells appear to lose their ability to reproduce themselves, and this may be the principal factor in temporary control of the tumor.

The place of regional chemotherapy in the treatment of human cancer remains to be determined. It is entirely possible that the desire for an agent as effective as aspirin and as free from toxic side-effects will be realized. Such a development would, of course, revolutionize the treatment of patients with cancer. On the other hand, assuming that the agents which are developed, while perhaps more effective therapeutically, will have toxic properties similar to those now in use, regional perfusion may be useful. From this series, it is clearly evident that regionally confined metastatic melanoma is significantly affected by the perfusion treatment; in fact, it is safe perhaps to conclude that it is the most effective therapy for patients with this disease in its recurrent or metastatic form. Its value as an adjunct to conventional surgical methods remains to be determined. At the other extreme the use of chemotherapeutic agents administered by perfusion for the treatment of patients with gastrointestinal carcinoma has been essentially without effect. Somewhat better response has been observed in the treatment of patients with carcinoma of the genitourinary tract, lung, and breast. While in no instance has an advanced lesion in these areas been arrested, significant palliation has been afforded in some cases and in others a nonresectable lesion has been converted to a resectable one. Furthermore, in almost every patient with pain resulting from far-advanced cancer, significant temporary relief of pain has been observed after treatment. With the agents now available, it is too much to expect that bulky tumors will be eradicated by chemotherapy, irrespective of the concentration of the agent and method of administration; yet it has been observed in this series that large, solid tumors shrink in size and undergo a considerable amount of necrosis. In the case of bulky lesions which are regionally confined, it is possible to induce peripheral necrosis and shrinkage of the lesion, thus making excision of the tumor feasible. In this way large, fungating, ulcerating lesions are removed and the patient may be rehabilitated, even though cure is not possible. For example, lower extremity perfusion was performed for metastatic melanomas in a patient who had been bedridden for two years. One of the lesions on the anterior part of the thigh weighed about 15 lb. and was ulcerating and foul. After perfusion and almost complete necrosis of this large lesion the residual base was excised and the area covered with a skin graft. Perfusion was performed again subsequently and the patient is now ambulant and relatively free of symptoms. The possibility that other lesions may appear later detracts in no way from the successful palliation achieved in this case.

The ease and safety with which perfusion can be repeated is gratifying. Lacking a "sensitivity test" it may be necessary to resort to trial of several agents administered at separate operations. In addition, retreatment of a responsive tumor is feasible, thereby increasing the opportunity for control of the lesion.

Insufficient experience with total-body perfusion has accumulated for proper evaluation. It is not certain that marrow replacement is necessary with the doses of nitrogen mustard used in this study. This and other aspects of total-body perfusion require investigation.

The use of perfusion techniques in the treatment of neural tumors may prove to be of importance. Although our experience with the treatment of tumors of this type is limited, Woodhall[5] and others are also investigating techniques for perfusing the brain, and an early evaluation of the effectiveness of this form of therapy may be possible.

Summary

Cancer chemotherapy with cytotoxic agents has the limitation of systemic toxicity, when large doses are used. Perfusion treatment is an attempt to diminish the toxic side-effects while permitting the use of larger doses of the cancericidal drugs. Perfusion techniques are of two types, regional and total-body. In the former, the effects of the drug are largely confined to the tumor-bearing area. In the latter, whole-body distribution of the agent occurs, but an attempt is made to minimize hematopoietic changes by autologous marrow transplantation. Techniques have been developed for regional perfusion of the extremities, pelvis, lungs, breast, oropharynx, and brain. The chemotherapeutic agents employed are nitrogen mustard, phenylalanine mustard, thio-TEPA, actinomycin-D, 5-fluorouracil, and a combined antimetabolite and alkylating agent (AB-100). Dosage of these agents varies with the area perfused, completeness of isolation, duration of action of the drug, and whether the patient has been given prior drug or x-ray therapy.

In the series reported, in 145 patients perfusion was performed 162 times for the treatment of cancer. There were 40 with malignant melanoma, 28 with sarcoma, 72 with carcinoma, and 4 with glioblastoma. Results of treatment have been evaluated in 120 cases. In 17 of the patients treatment was adjunctive to surgical excision of a primary tumor, and in 103 it was attempted for palliation of far-advanced cancer. In 55 the lesions are quiescent, in 27 there has been temporary regression of the tumor, followed by recurrent growth, and in 30 perfusion was without effect. There were eight operative deaths. Complications consisted of edema and discoloration of the perfused area and depression of hematopoiesis. In most instances these complications were not serious and responded promptly to therapy. Regional perfusion for malignant melanoma appears to be effective in the treatment of patients with recurrent or metastatic lesions. The value of perfusion in the treatment of patients with other types of tumors is not yet clear.

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The place of regional chemotherapy in the treatment of human cancer remains to be determined. It is entirely possible that the desire for an agent as effective as aspirin and as free from toxic side-effects will be realized. Such a development would, of course, revolutionize the treatment of patients with cancer. On the other hand, assuming that the agents which are developed, while perhaps more effective therapeutically, will have toxic properties similar to those now in use, regional perfusion may be useful. From this series, it is clearly evident that regionally confined metastatic melanoma is significantly affected by the perfusion treatment; in fact, it is safe perhaps to conclude that it is the most effective therapy for patients with this disease in its recurrent or metastatic form. Its value as an adjunct to conventional surgical methods remains to be determined. At the other extreme the use of chemotherapeutic agents administered by perfusion for the treatment of patients with gastrointestinal carcinoma has been essentially without effect. Somewhat better response has been observed in the treatment of patients with carcinoma of the genitourinary tract, lung, and breast. While in no instance has an advanced lesion in these areas been arrested, significant palliation has been afforded in some cases and in others a nonresectable lesion has been converted to a resectable one. Furthermore, in almost every patient with pain resulting from far-advanced cancer, significant temporary relief of pain has been observed after treatment. With the agents now available, it is too much to expect that bulky tumors will be eradicated by chemotherapy, irrespective of the concentration of the agent and method of administration; yet it has been observed in this series that large, solid tumors shrink in size and undergo a considerable amount of necrosis. In the case of bulky lesions which are regionally confined, it is possible to induce peripheral necrosis and shrinkage of the lesion, thus making excision of the tumor feasible. In this way large, fungating, ulcerating lesions are removed and the patient may be rehabilitated, even though cure is not possible. For example, lower extremity perfusion was performed for metastatic melanomas in a patient who had been bedridden for two years. One of the lesions on the anterior part of the thigh weighed about 15 lb. and was ulcerating and foul. After perfusion and almost complete necrosis of this large lesion the residual base was excised and the area covered with a skin graft. Perfusion was performed again subsequently and the patient is now ambulant and relatively free of symptoms. The possibility that other lesions may appear later detracts in no way from the successful palliation achieved in this case.

The ease and safety with which perfusion can be repeated is gratifying. Lacking a "sensitivity test" it may be necessary to resort to trial of several agents administered at separate operations. In addition, retreatment of a responsive tumor is feasible, thereby increasing the opportunity for control of the lesion.

Insufficient experience with total-body perfusion has accumulated for proper evaluation. It is not certain that marrow replacement is necessary with the doses of nitrogen mustard used in this study. This and other aspects of total-body perfusion require investigation.

The use of perfusion techniques in the treatment of neural tumors may prove to be of importance. Although our experience with the treatment of tumors of this type is limited, Woodhall[5] and others are also investigating techniques for perfusing the brain, and an early evaluation of the effectiveness of this form of therapy may be possible.

Summary

Cancer chemotherapy with cytotoxic agents has the limitation of systemic toxicity, when large doses are used. Perfusion treatment is an attempt to diminish the toxic side-effects while permitting the use of larger doses of the cancericidal drugs. Perfusion techniques are of two types, regional and total-body. In the former, the effects of the drug are largely confined to the tumor-bearing area. In the latter, whole-body distribution of the agent occurs, but an attempt is made to minimize hematopoietic changes by autologous marrow transplantation. Techniques have been developed for regional perfusion of the extremities, pelvis, lungs, breast, oropharynx, and brain. The chemotherapeutic agents employed are nitrogen mustard, phenylalanine mustard, thio-TEPA, actinomycin-D, 5-fluorouracil, and a combined antimetabolite and alkylating agent (AB-100). Dosage of these agents varies with the area perfused, completeness of isolation, duration of action of the drug, and whether the patient has been given prior drug or x-ray therapy.

In the series reported, in 145 patients perfusion was performed 162 times for the treatment of cancer. There were 40 with malignant melanoma, 28 with sarcoma, 72 with carcinoma, and 4 with glioblastoma. Results of treatment have been evaluated in 120 cases. In 17 of the patients treatment was adjunctive to surgical excision of a primary tumor, and in 103 it was attempted for palliation of far-advanced cancer. In 55 the lesions are quiescent, in 27 there has been temporary regression of the tumor, followed by recurrent growth, and in 30 perfusion was without effect. There were eight operative deaths. Complications consisted of edema and discoloration of the perfused area and depression of hematopoiesis. In most instances these complications were not serious and responded promptly to therapy. Regional perfusion for malignant melanoma appears to be effective in the treatment of patients with recurrent or metastatic lesions. The value of perfusion in the treatment of patients with other types of tumors is not yet clear.

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Laboratory Data in Patient with Myopathy and Hypercalcemia Occurring with Carcinoma of the Kidney

Date	Serum Calcium Level, Mg. %	Serum Phosphorus Level, Mg. %	Alkaline Phosphatase Level, Bodansky Units	Acid Phosphatase Level, King-Armstrong Units	Blood Urea Nitrogen Level, Mg. %
7/17	..	..	..	..	20
7/21	..	2.9	2.4	..	..
7/23	..	3.1	..	0.1	..
7/25	11.4	2.0	..	..	..
8/3	11.3	..	..	..	..
8/4	..	2.8	2.5	0.3	..
8/8*	..	..	..	..	20
8/9	8.8	3.2	..	..	..
8/13	8.8	3.0	1.3	0.1	11.5
8/22	8.6	..	..	..	..
9/12	10.6	..	20†	..	19.5

* Nephrectomy was performed on 8/6.
† King-Armstrong units (normal values = 4 to 12 units).

A roentgenogram of the chest showed no abormality. A film of the pelvis showed considerable icrease in density of the left innominate bone ith preservation of the trabecular pattern, sugesting osteitis deformans (Paget's disease). Films f the skull, spine, and femurs showed no lesions. ntravenous pyelography showed distortion of the pper pole of the right kidney (fig. 1).

Lumbar puncture yielded clear spinal fluid under ormal pressure. No cells were present in the fluid, nd the total protein level was 24 mg.%. The pinal fluid test and blood serologic test for syphilis ave negative results. A needle biopsy specimen f the prostate showed benign hyperplasia of the land. Bone biopsy specimens from the left ilium howed changes compatible with osteitis deformans nd no evidence of metastatic tumor. Muscle biopsy specimens from the right quadriceps femoris howed marked atrophy of individual muscle fibers ith areas of fibrinoid degeneration of the sarcolasm. Prominent infiltration of the muscle tissue y chronic inflammatory cells was present, and the istological architecture was almost totally detroyed (fig. 2).

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Postoperatively the patient showed rapid recovry of strength and was able to sit up unassisted ne week after the operation. He could walk quite ell with slight support from a cane three weeks after the operation. When he returned for reevaluation four and one-half months after operation, he appeared quite well and had gained 28 lb. (12.7 kg.). The general physical examination was not remarkable. Muscle strength showed return to an almost normal level in all groups. His gait was erect and hand strength was good. The deep tendon reflexes were still absent in the legs and minimal decrease to vibratory sense was present in the right foot. Sensation for pinprick and light touch was normal.

The hemogram and urinalysis showed normal findings. The serum calcium level was 10.6 mg.%, alkaline phosphatase level 20 King-Armstrong units, and blood urea nitrogen level 19.5 mg.%. A chest roentgenogram showed the presence of a density at the left hilus, measuring 3 by 5 cm., and a smaller density in the right lung field. Both of these lesions had appeared since the previous admission and were thought almost certainly to be metastases. A muscle biopsy specimen from the right quadriceps femoris showed atrophy of the muscle fibers. No fibrinoid degeneration was present in this specimen (fig. 5).

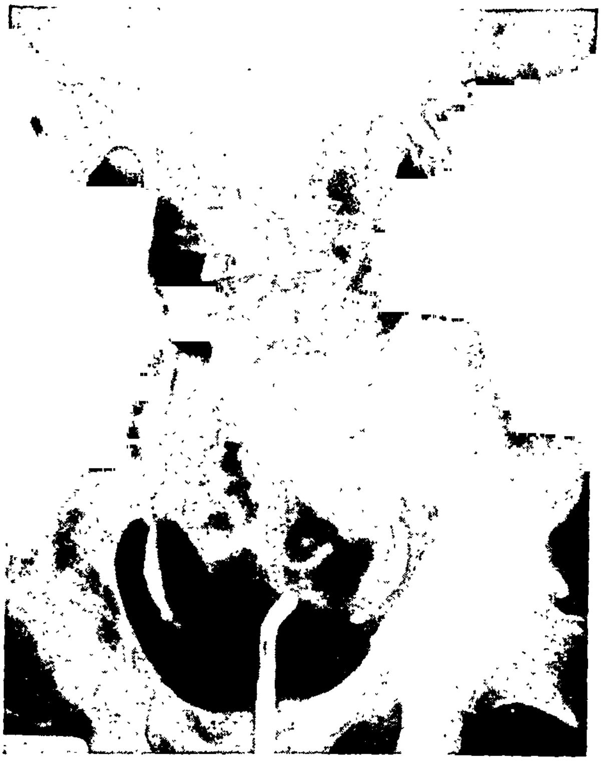

Fig. 1.—Retrograde pyelogram showing filling defect at superior pole of right kidney and osteoblastic activity in left innominate bone.

Comment

A multiplicity of neurological and muscular disorders have been described in accompaniment with carcinoma. The more common patterns of

MYOPATHY AND HYPERCALCEMIA OCCURRING WITH CARCINOMA OF THE KIDNEY

Bernardo F. Alanis, M.D.
and
John F. Flanagan, M.D., Durham, N. C.

In this case of a 63-year-old man the essential complaint during the first three months of illness was muscular weakness, affecting especially the legs and progressing to complete disability. Later symptoms led to surgical removal of the right kidney and diagnosis of clear-cell carcinoma. The nephrectomy was followed by improvement in neuromuscular status until muscle strength had returned to almost normal. Deep reflexes in the legs did not return, and biopsy of the quadriceps femoris muscle revealed extensive atrophy. Hypercalcemia was detected before operation and subsided thereafter; its time-relation to other blood-chemical findings, to the neuromuscular disturbance, to osteoblastic activity manifested in the bones, and to the ultimate appearance of masses in both lungs suggests that calcium played a central role in the symptomatology of this patient.

The occurrence of neuromuscular diseases in association with malignant tumors has become a well-recognized entity in the past 10 years. A few reports[1] of neurological disorders accompanying carcinoma appeared many years ago. In 1948 Denny-Brown[2] reported two cases of peripheral neuropathy associated with carcinoma of the lung, and interest was reawakened in this syndrome. Later, the excellent papers of Brain, Henson, and others[3] defined quite well the clinical and pathological characteristics of the varied neurological and muscular disorders which have appeared in association with carcinoma.

In most of the reported cases,[3] the primary neoplasm originated in the lungs. The syndrome has also been reported with carcinoma of the prostate, ovary, rectum, and breast and in cases where the primary site of malignancy could not be determined.[3h] To our knowledge no previous report has appeared in which neuromuscular disease was associated with carcinoma of the kidney. The present case report also appears to be noteworthy because of the presence of hypercalcemia and hypophosphatemia preoperatively.

Report of a Case

A 63-year-old man was admitted to the Durham Veterans Administration Hospital on July 17, 1958, because of severe generalized muscle weakness of four months' duration. The patient had been perfectly well until January, 1958, when he began to notice progressive weakness in the legs on attempting to arise from a sitting position or on ascending steps. Slapping gait with drop foot and failure of muscle strength in the arms appeared shortly thereafter. The weakness was primarily in the proximal muscles, but weakness of handgrip was present also. Three months after the onset of progressive muscle weakness the patient developed colicky pain in the right flank which was thought to be due to passage of a renal calculus. The same type of flank pain recurred one month later, and the patient was hospitalized elsewhere for evaluation. He remained bedfast and became unable to raise his arms sufficiently to feed himself. He was transferred to the Durham Veterans Administration Hospital on July 17, 1958. Throughout the course of his illness he had lost 44 lb. (20 kg.).

On physical examination, the patient was a euphoric 63-year-old man, with blood pressure 130/70 mm. Hg, pulse rate 76 per minute, and temperature 98.6 F (37 C). The skin showed bilateral palmar erythema. Extreme weakness and wasting of the muscles of the extremities was present. The patient was unable to sit unassisted or to extend his arms above the bed. The handgrip was weak but not as markedly reduced in strength as the proximal muscle power. The deep tendon reflexes were normal in the arms and were totally absent in the legs. The cremasteric reflexes were absent. Plantar response was downward on the right and of withdrawal character on the left. Sensory examination showed no deficit to pinprick, position, or vibration. Tingling dysesthesia to sensory stimulation of the feet was noted by one observer. The remainder of the physical examination was noncontributory.

Initial laboratory data showed the hemoglobin level to be 12.0 Gm.% and white blood cell count 9,800 per cubic millimeter. The urinalysis showed a faint trace of protein and 0 to 3 white blood cells per high-power field. The blood urea nitrogen level was 20 mg.%. Serum sodium, chloride, and potassium levels and carbon dioxide-combining

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power value were normal. The alkaline phosphatase level was 2.4 Bodansky units, and the acid phosphatase level was 0.1 King-Armstrong units. Eight days after the patient's admission the serum calcium level was 11.4 and the serum phosphorus level 2.0 mg.%. (Subsequent values are shown in the table.)

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8/5*	..	..	..	..	20
8/9	8.8	3.2	..	..	..
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* Nephrectomy was performed on 8/6.
† King-Armstrong units (normal values = 4 to 12 units).

A roentgenogram of the chest showed no abnormality. A film of the pelvis showed considerable increase in density of the left innominate bone with preservation of the trabecular pattern, suggesting osteitis deformans (Paget's disease). Films of the skull, spine, and femurs showed no lesions. Intravenous pyelography showed distortion of the upper pole of the right kidney (fig. 1).

Lumbar puncture yielded clear spinal fluid under normal pressure. No cells were present in the fluid, and the total protein level was 24 mg.%. The spinal fluid test and blood serologic test for syphilis gave negative results. A needle biopsy specimen of the prostate showed benign hyperplasia of the gland. Bone biopsy specimens from the left ilium showed changes compatible with osteitis deformans and no evidence of metastatic tumor. Muscle biopsy specimens from the right quadriceps femoris showed marked atrophy of individual muscle fibers with areas of fibrinoid degeneration of the sarcoplasm. Prominent infiltration of the muscle tissue by chronic inflammatory cells was present, and the histological architecture was almost totally destroyed (fig. 2).

A right nephrectomy was performed three weeks after admission of the patient. Pathological examination showed replacement of the upper one-half of the kidney by a partially necrotic gray tumor measuring 10 cm. in diameter (fig. 3). Histologically the tumor was a typical clear-cell carcinoma of the kidney (fig. 4).

Postoperatively the patient showed rapid recovery of strength and was able to sit up unassisted one week after the operation. He could walk quite well with slight support from a cane three weeks after the operation. When he returned for reevaluation four and one-half months after operation, he appeared quite well and had gained 28 lb. (12.7 kg.). The general physical examination was not remarkable. Muscle strength showed return to an almost normal level in all groups. His gait was erect and hand strength was good. The deep tendon reflexes were still absent in the legs and minimal decrease to vibratory sense was present in the right foot. Sensation for pinprick and light touch was normal.

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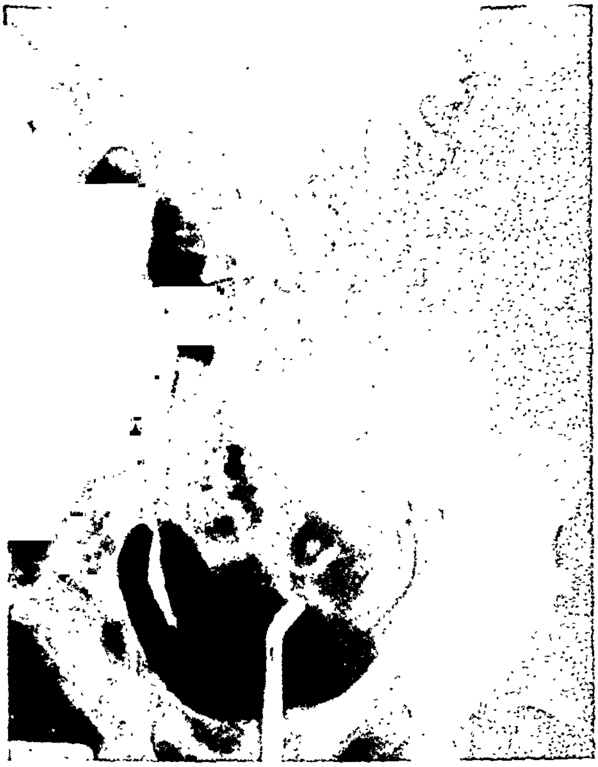

Fig. 1.—Retrograde pyelogram showing filling defect at superior pole of right kidney and osteoblastic activity in left innominate bone.

Comment

A multiplicity of neurological and muscular disorders have been described in accompaniment with carcinoma. The more common patterns of neurological disturbance have fallen into four groups [3c]: (1) cortical and cerebellar degeneration in which ataxia, Babinski responses, adventitious movements, diplopia, and nystagmus have been the predominant findings; (2) mixed motor and sensory syndromes, with marked loss of muscle substance, weakness, decrease of deep tendon reflexes, and loss of position and vibration sense; (3) virtually pure sensory neuropathy; and (4) pure myopathy.

Our patient appeared to possess a predominantly myopathic illness. Complete absence of the deep tendon reflexes in the legs and absence of the cremasteric reflex persisted after good recovery of muscle strength had taken place, suggesting that there was also a neuropathic component to the illness.

Autopsy studies in the patients reported in the literature have shown multiple degenerative lesions in the cerebellum, medulla, dorsal root ganglions, and motor cells of the spinal cord.[4] In the patients with pure myopathy, severe degenerative changes of nonspecific nature have been found in the involved muscles.[3c]

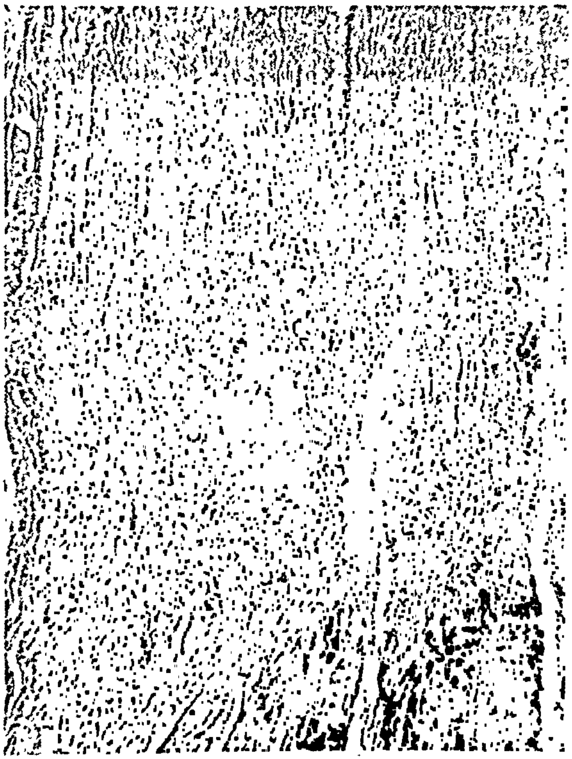

Fig. 2.—Biopsy specimen of quadriceps femoris muscle prior to nephrectomy showing complete loss of muscle architecture, fibrosis, and chronic inflammatory cell infiltration. Single markedly degenerated muscle fiber is present in center of picture (× 69).

The course of these neurological and myopathic illnesses has been quite unpredictable in most cases. Occasional patients have shown improvement after removal of the primary tumor, but in most instances the neurological symptoms have pursued a course independent of the progress of the malignancy. Quite often the neurological symptoms have shown spontaneous improvement at a time when the patient was entering a terminal phase of carcinomatous cachexia.[4]

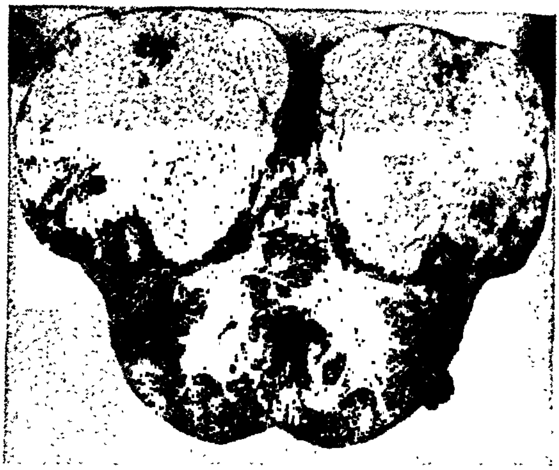

Fig. 3.—Section of right kidney showing replacement of upper pole by carcinoma.

Speculation has arisen in regard to the pathogenesis of these disorders of the nervous system. Possible etiological factors which have been mentioned include production of a neurotoxic substance by the tumors, autosensitization to tumor protein, and nutritional deficiency due to the presence of a malignant tumor. Investigation [3] has yielded no convincing support for any of these opinions as yet.

The relationship of myopathy to the purely neurological syndromes has been a source of debate. Adams and associates [5] continue to look on the myopathic form as a type of chronic polymyositis. Brain and Henson [3b] have been impressed by the marked diminution of deep tendon reflexes and superficial reflexes and believe that the evidence is sufficient to suggest that the myopathy represents a neuromuscular disorder.

The second remarkable feature of the case reported here was the presence of hypercalcemia prior to operation in the absence of recognizable metastases to the bone. Serum calcium levels of 11.3 and 11.4 mg.% were encountered before operation. Five days after operation the serum calcium level had fallen to 8.8 mg.%. Serum phosphorus levels were low prior to operation and remained at the lower limit of normal after operation. Alkaline and acid phosphatase determinations were normal at the time of operation, but, on reevaluation four and one-half months after operation, the alkaline phosphatase level had risen to 20 King-Armstrong units.

The occurrence of hypercalcemia in association with malignant tumors has been reported previously. Plimpton and Gellhorn [6] described 10 cases of hypercalcemia accompanying malignant tumors in which no major bony metastases were present. Four of these patients had carcinoma of the kidney (three of the clear-cell type and one of unspecified type). Only 3 of the 10 patients were in an operable state at the time they came under observation. Two of the operable patients had carcinoma of the kidney, and in both the serum calcium level rapidly fell to normal after operation. The third patient, with adenocarcinoma of the ovary, showed a prompt fall in the calcium level after operation, but the hypercalcemia reappeared when local recurrence of the tumor developed. Our patient was similar to these patients in that his serum calcium level fell to normal five days after operation. Four and one-half months later, the serum calcium level was still normal though evidence of metastases in the lungs had appeared. At that time the serum alkaline phosphatase level had risen to 20 King-Armstrong units.

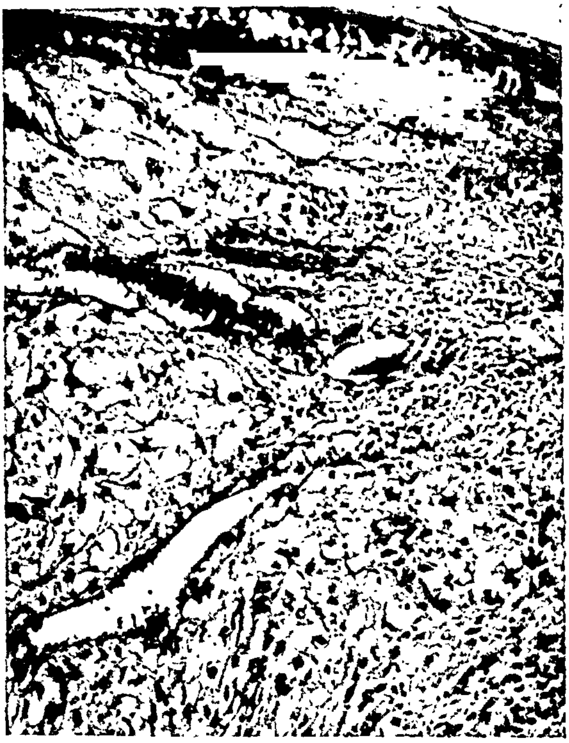

Fig. 4.—Histological section of renal tumor. Typical clear-cell carcinoma pattern is present. Necrosis of tumor with infiltration by polymorphonuclear cells is shown.

The precise etiology of hypercalcemia accompanying malignant tumors without bone involvement has not been defined.[7] Thomas and associates[7a] showed that the characteristic findings in this syndrome are hypercalcemia of variable degree, hypophosphatemia, and decreased tubular reabsorption of phosphorus. The response of their patients to corticosteroid administration was found to be quite inconsistent, and these workers concluded that the corticosteroid test was of little value in distinguishing the hypercalcemia of malignant disease from true hyperparathyroidism. Histological examination of the parathyroid glands in patients with elevated blood calcium levels and malignant tumors has been unrevealing for the most part, though mild hyperplasia of these glands was seen in one of the reported cases.[8] Elucidation of the origin of hypercalcemia in malignancy must await further study.

In our patient the possibility exists that the entire picture of severe muscle weakness and wasting was due solely to the presence of hypercalcemia. In hyperparathyroidism, marked hypercalcemia may be associated with considerable impairment of muscle strength[9]; in the experimental animal, hypercalcemia has been found to be accompanied by frank necrosis of muscle fibers.[10] In both of these situations the recorded blood calcium values were considerably higher than the ones present in our patient. Accordingly, it seems most unlikely that the modest degree of hypercalcemia seen in this case was sufficient to explain the profound degree of muscle weakness and degeneration.

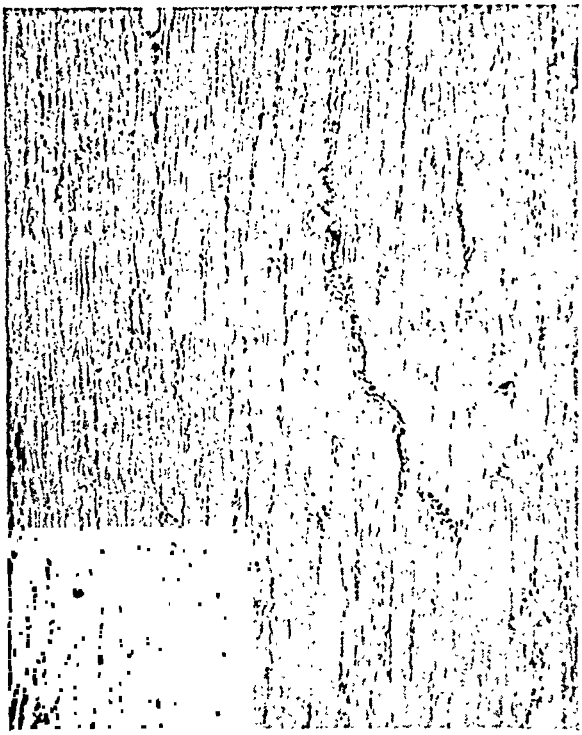

Fig. 5.—Biopsy specimen of quadriceps femoris muscle after nephrectomy showing atrophy of muscle and loss of striations (× 69).

Interpretation of the findings in this patient is further complicated by the presence of osteoblastic activity in the pelvic bones. The roentgenogram and bone biopsy specimen of this lesion showed characteristics of osteitis deformans. Since operative removal of the tumor was followed by prompt fall in the blood calcium level, we believe that the relationship of tumor to hypercalcemia is fairly clear. It seems reasonable to assume that osteitis deformans was of little importance in this relationship.

Summary

Myopathy and hypercalcemia occurred in a patient with clear-cell carcinoma of the kidney. Progressive generalized skeletal muscle weakness preceded the appearance of hematuria by three months. After operative removal of the renal tumor the patient showed remarkable improvement of muscle strength and the blood calcium levels returned to normal. The patient was asymptomatic four and one-half months after operation, although the chest roentgenogram showed the appearance of masses in both lung fields since the previous admission.

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CLINICAL DIAGNOSIS OF TRACHEAL ADENOMA (CYLINDROMA)

REPORT OF A CASE

A. Irwin Kleinman, M.D.
and
Ida Levine, M.D., Brooklyn, N. Y.

The presenting symptoms in patients with tracheal tumors may be those commonly associated with bronchial asthma. Such a clinical picture is illustrated in the following case report.

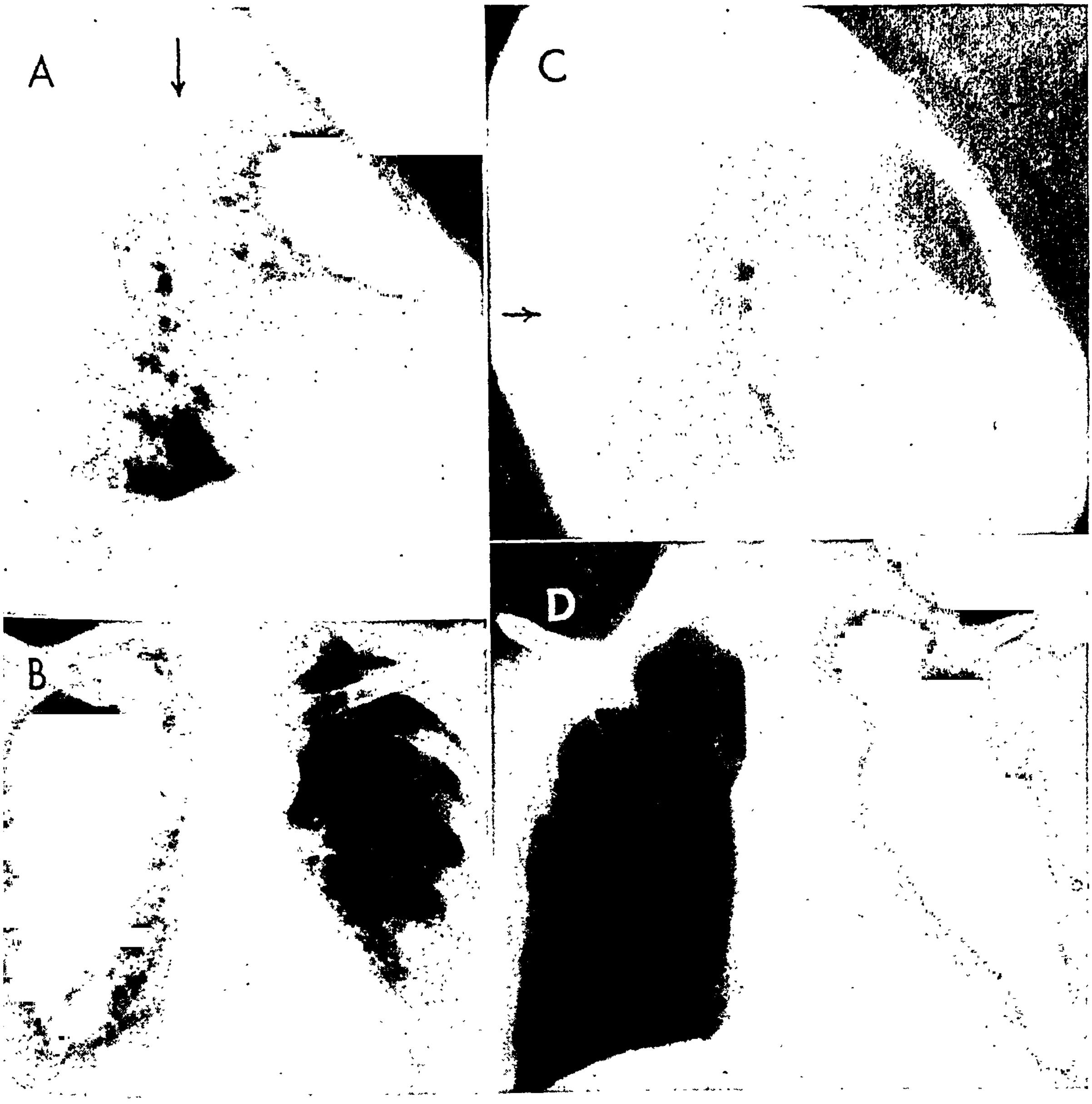
A 48-year-old woman was admitted to the Beth-El Hospital on Jan. 17, 1959, because of respiratory difficulty. She had been well until 1947, when she suffered an attack of bronchopneumonia. Since then she had developed wheezing respiration and had had two or three severe lung infections each year. Her sputum consisted of a scant white or grayish mucoid material, except for insignificant blood-streaking whenever her cough was severe. These minimal hemoptyses had antedated her attack of pneumonia by six years, and the most recent attack had occurred three days prior to admission.

In 1950, because of peripheral blood eosinophilia (8%) and a sputum specimen containing many eosinophils, the patient was referred to one of us (A. I. K.) for therapy. She was found to be very sensitive to any strong odor, and she had positive results for skin tests to house dust and a number of foods. An antiallergen regimen was prescribed—that is, house-dust and autogenous vaccine (sputum) injections, dust precautions, and elimination of positively reacting foods. She was given antibiotics as needed to combat her pulmonary infections.

Nevertheless, at various times during her office visits, it was noted that her wheezing persisted and tended to be more inspiratory than expiratory.

Associate Attending Allergist (Dr. Kleinman) and Associate-in-Charge, Thoracic Service (Dr. Levine), Beth-El Hospital.

Roentgenograms of the chest were taken repeatedly and all were interpreted as within normal limits, with a single exception. A lateral chest roentgenogram taken in 1950 suggested the possibility of a tracheal lesion, emphysema, and osteoarthritis of e thoracic region of the spine (see figure, *A*). ronchoscopy was done immediately, and negative sults were reported.



A, lateral roentgenogram of chest, taken May 9, 1950. Arrow indicates possible intratracheal density. *B*, posteroanterior entgenogram of chest, taken Jan. 19, 1959. No lesion is discernible. *C*, lateral roentgenogram of chest, taken Jan. 23, 1959. ssible intratracheal lesion is again seen. Compression of vertebral body is indicated by arrow. *D*, tomogram of chest at 9-cm. el, Jan. 23, 1959. Intratracheal tumor is demonstrated.

She continued to wheeze, and her chest circumrence, as measured by her brassiere, increased 4 . in size between 1950 and 1959. In September, 958, her inspiratory stridor was so severe that ronchoscopy was again performed. The bronchoscopist found a profuse amount of thick mucoid material. Aspiration of this resulted in considerable temporary relief. Subsequently, her asthmatoid breathing became worse and finally led to her most recent hospitalization.

Physical examination on admission showed an apprehensive woman whose respirations were rapid and so noisy they could be heard from the doorway of her room. She was not orthopneic. With each inspiration a deep suprasternal retraction took place. Her expiration time was not prolonged. Bilateral wheezing and rhonchi could be heard throughout respiration anteriorly and posteriorly.

Her chest was barrel-shaped, with a tendency to kyphosis. Otherwise the physical examination and laboratory tests showed negative results, except for a white blood cell count of 12,000 per cubic millimeter and an increased sedimentation rate of 36 mm. per hour (Wintrobe). Her posteroanterior chest film showed negative findings (see figure, *B*).

Clinically she had the classic signs of an obstruction above the tracheal carina. Lateral films and tomograms were then taken, and the diagnosis of a tracheal adenoma became obvious (see figure, *C* and *D*). There was again seen the abnormality of the thoracic vertebrae, but there was no uniformity of opinion as to whether this represented metastatic disease. A rounded density at the base of the right lung was also present.

Removal of the tracheal lesion was considered urgent, and on Jan. 28, 1959, an operation was performed by Dr. Charles Ripstein, director of surgery, Beth-El Hospital. The sternum was split in the midline, the trachea opened, and 4 cm. above the carina a smoothly covered mass (1 by 1 by 1.8 cm.) arising from a narrow stalk on the right posterolateral wall was removed uneventfully. Her respiratory difficulty cleared immediately and no further wheezing could be heard. The patient was discharged on Feb. 8. The histopathological report was "infiltrating adenoma of the trachea which histologically is a mucoepidermoid variant of cylindroma with many atypical cells."

The patient has continued to be free of pulmonary complaints to the time of her most recent examination (Aug. 27, 1959). She was not dyspneic and did not wheeze. She had no complaints referable to her spine. If indolent metastases were present, they were still asymptomatic in nature.

Comment

This is a case of an allergic person whose symptoms of wheezing and dyspnea were not completely typical of asthma in that inspiratory stridor was present, and who in fact had a mechanical obstruction due to a tracheal adenoma. The intermittent symptoms may be explained by variation in the size of the tumor, depending on the degree of infectious or allergic swelling. The diagnosis became obvious when tomography was done. The suspension of the tumor by a narrow stalk probably explains why it was not discovered during two bronchoscopies.

The 18-year history of minimal hemoptysis and the 12-year history of asthmatic breathing fit very well with the recorded difficulty in diagnosing cylindromas. Cylindromas, whether of the parotid,[1] the breast,[2] or the trachea,[3] are notorious for their late diagnosis. Their metastases are also late and slow growing. The rarity[4] of this low-grade malignancy need not excuse the delay in diagnosis. Use of all available facilities of study can minimize the handicap of rarity. We present this report as a plea for early tomography in any puzzling case of inspiratory stridor or atypical asthma.

232 Lincoln Pl. (17) (Dr. Kleinman).

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CARBON DIOXIDE VERSUS OXYGEN FOR DIAGNOSTIC STUDIES.—Occasional reports of gas embolism with fatal results following the use of air or oxygen in diagnostic Rubin tests led to . . . the use of the more soluble gas, carbon dioxide, as the insufflating agent. Nevertheless, in spite of the widespread acceptance of the hazards involved, air and oxygen continue to be used commonly for tubal insufflation as well as for diagnostic air contrast studies in the practice of urology and surgery. . . . The median lethal doses of intravenous air and carbon dioxide were determined in 89 mongrel dogs. This study showed that air is approximately five times as toxic as carbon dioxide as an intravenous embolic agent. . . . The relative toxicity differential between the two gases in laboratory animals is offered as evidence for the preferential use of carbon dioxide as an insufflating or gas contrast material in clinical practice.—T. D. Graff, M.D., N. R. Arbegast, M.D., O. C. Phillips, M.D., and others, Gas Embolism: A Comparative Study of Air and Carbon Dioxide as Embolic Agents in the Systemic Venous System, *American Journal of Obstetrics and Gynecology*, August, 1959.

GIANT PIGMENTED NEVI

James L. Russell, M.D.
and
Raul G. Reyes, M.D., New Orleans

Giant pigmented nevi fortunately are uncommon. There have been about 53 cases reported in the literature. The nevus unius lateris as reported by Pack and Sunderland [1] is believed to represent a different clinical and pathological entity. To the 53 cases enumerated we would like to add another which was treated surgically. To our knowledge this nevus represents the largest which has been completely and successfully resected.

Report of a Case

The patient, an 18-year-old girl, first presented herself at Charity Hospital on Sept. 15, 1953, with a giant pigmented nevus which covered her entire back and myriads of small nevi over the remaining body surface (fig. 1). Her principal complaint was that the large lesion emitted a foul odor (due to intermittent ulceration and infection). She also complained of pain and pruritus. The nevus was infected at the time of admission and had been for about three to four weeks. The infection was resistant to local hygienic measures but had healed on a previous occasion after prolonged care.

She was the third of four children in a family in which all were living and well. The mother and one of the siblings have scattered small nevi over their bodies, but no familial or hereditary trait for the giant nevus was evident.

Her birth was a normal spontaneous delivery. The mother gave no history of any unusual prenatal experiences or diseases. The nevus was present at the time of birth and covered her entire back. She was hospitalized for 20 days after birth, during which time the mother stated that radiation therapy was attempted to control the lesion. No appreciable change occurred after this treatment.

The nevus grew and increased in size relative to the normal growth and development of her body. When the patient was 8 years of age a few of the smaller nevi were removed surgically, but the larger lesion was undisturbed. Her last evaluation by a physician was at 13 years of age when numerous small nevi were destroyed by electrocautery. At this time she was again advised against surgery for the large nevus. When she reached the age of puberty, there was no noticeable change in the lesion, although she became more conscious of its presence and infection became a troublesome factor.

Giant pigmented nevi afflict the patient not only with an unsightly cosmetic defect but also with the hazard of possible conversion to cancer. Such a nevus, extending over the back of an 18-year-old girl, was removed by surgical excision. Several hundred smaller nevi were removed from other parts of her body surface. Three separate operative procedures were required; the first was to remove the nevi from the right side of her body and prepare a skin donor site, the second to remove part of the large nevus and the smaller ones from her left side, and a third for complete excision of the giant nevus. Almost all the skin grafts were successful, and no malignant changes were found in any of the nevi excised.

Psychologically she was well adjusted to her cosmetic handicap, although she still found it necessary to keep the lesion constantly concealed. She and her mother both were resigned to the fact that this grotesque disfigurement was irremediable.

Physical examination revealed that she was well developed, well nourished, and of average weight and height. Her back was covered almost entirely by one enormous pigmented hairy nevus which extended from the level of the seventh cervical vertebra, inferiorly, to the level of the lumbosacral junction, a distance of 42 cm. Laterally it extended from one posterior axillary line to the opposite, a distance of 40 cm. The lesion was sharply demarcated from the surrounding normal tissue, not only because of its brownish-black color but also by its elevation, which varied in different areas from 1 to 3 cm. This thickness of the lesion imparted to it a soft and elastic consistency similar to a plexiform neurofibroma. The verrucous surface was marked by numerous papillary excrescences and deep fissures and was covered by an abundant growth of black hair. Exfoliation of friable pieces of the tumor occurred constantly. Over the left scapular region there was an area of ulceration and infection covered by a fibropurulent exudate. No palpable lymph nodes were present in the axilla or elsewhere.

Several hundred small satellite nevi covered her entire body surface (fig. 1). They varied in size, configuration, and color. Some were warty and covered with hair (the nevus pilosus verrucosus);

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others, such as those found on the palms of the hands and soles of the feet, were flat (nevus spillus). A number of circular scars containing pigment were dispersed over both legs and thighs. These represented sites of inadequate cauterization with residual nevus cells scattered in the scar tissue.

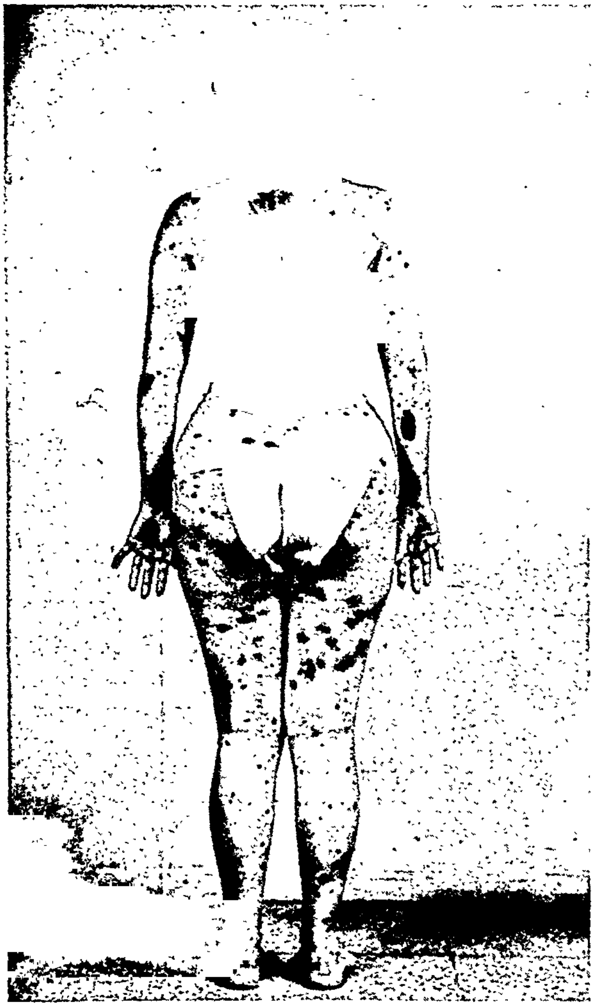

Fig. 1.—Patient aged 18 showing gigantic nevus and multiple satellite nevi over entire body.

The patient was prepared for surgery Sept. 28, 1953. The first procedure consisted of excision of multiple small nevi over the right side of the body. This included the palm of the hand, the sole of the foot, the entire thigh, the leg, where incomplete cauterization had been performed, and the right side of the abdomen. The rationale for proceeding in this manner was to remove all the precancerous lesions first, while at the same time preparing a donor site. It was also undesirable to completely incapacitate the patient by operating on both hands and feet simultaneously. In this way she could be ambulatory two or three days after surgery. A general anesthesia was administered, and with two surgical teams at work about 200 nevi were elliptically excised and closed primarily. On Oct. 10, 1953, a similar procedure was performed on the opposite side.

After a short leave from the hospital she was readmitted for a third operation which was performed Nov. 10, 1953. Under endotracheal anesthesia three large strips of skin of about 17/1,000 in. in thickness, 40 cm. in length, and 8 cm. in width were removed with a vacuotome from the left thigh. Her position was changed, and about one-third of the lesion was excised and grafted. An estimated 95% take of the grafts was noted. She was discharged from the hospital two weeks after surgery.

Her final surgical procedure took place Jan. 12, 1954, at which time the remainder of the lesion was excised. Four strips of split-thickness skin, taken from the right thigh, were used to reconstruct the area. One hundred per cent acceptance of the grafts occurred. Healing was rapid, and was followed by a course of physical therapy and oil massage.

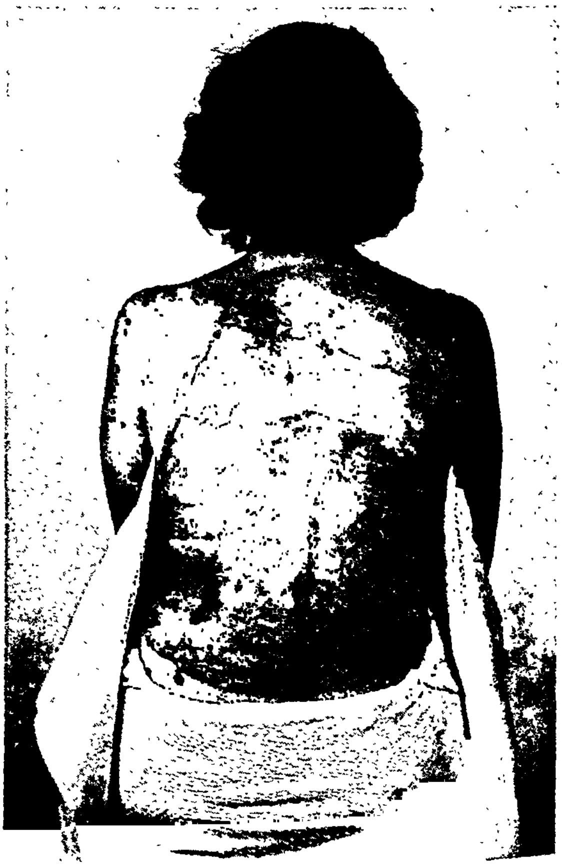

Fig. 2.—Photograph taken May, 1954, five months after final procedure, showing complete healing.

The patient was photographed when last seen in May, 1954 (fig. 2). The area was covered by soft, pliable, freely movable skin with only slightly abnormal sensation. She was more than well satisfied with the results, and her mental outlook had markedly improved.

Histopathology.—Representative sections were taken from various portions of the giant nevus for microscopic study. In general, the histological picture conformed throughout with few exceptions. Study of the epidermal layer revealed an irregular, verrucous surface covered by an atrophic, hyperkeratotic, stratified squamous epithelium. The continuity of the epidermis-cutis junction was uninterrupted in most sections, but increased cellular activity was noted in one specific area in the stratum spinosum. Here spherical aggregations of melanoblasts surrounded by a residual wall of epidermal cells were poised at the epidermis-cutis junction in apparent readiness to detach themselves and enter the underlying stroma (fig. 3). This was the only evidence of junctional activity seen in the sections. Immediately beneath the epidermis, nevus cells were seen in varying arrangements. More superficially they were grouped as elongated cords or oval clusters (fig. 4). They also were found in solid sheets or scattered individually throughout the stroma. In the deeper layers of the dermis and subcutaneous tissues was found a gradual transition of the nevus cell from the more polygonal cell of the papillary layer to a cell resembling a fibroblast or Schwann cell (fig. 5).

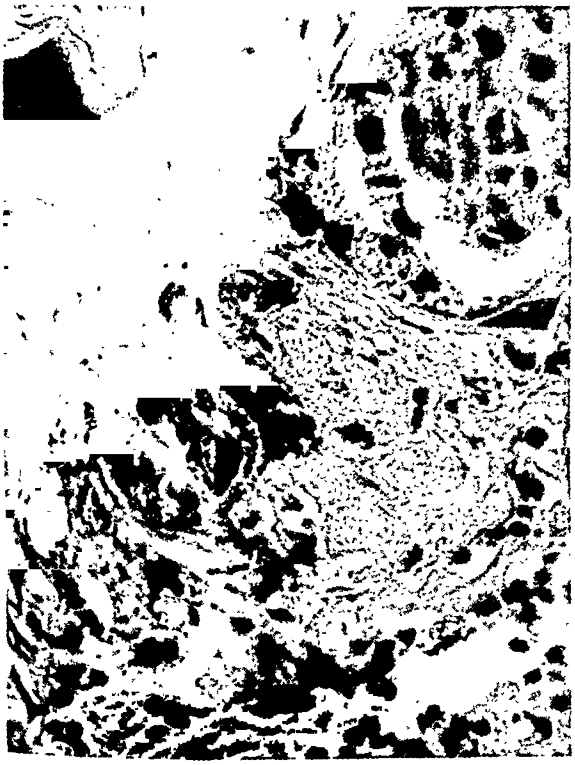

Fig. 3.—Photomicrograph under high-power magnification showing junctional activity. Note aggregations of melanoblasts with central group breaking into dermis.

The diagnosis was giant compound neuronevus and multiple neuronevi, predominantly intradermal, with some junctional components.

Management

Generally speaking, all giant pigmented nevi should be surgically removed; not only to overcome the cosmetic blemish but to avoid the possible future hazard of degeneration or malignant transformation. There will be but few cases that fall into the categorically inoperable class because of their extensiveness.

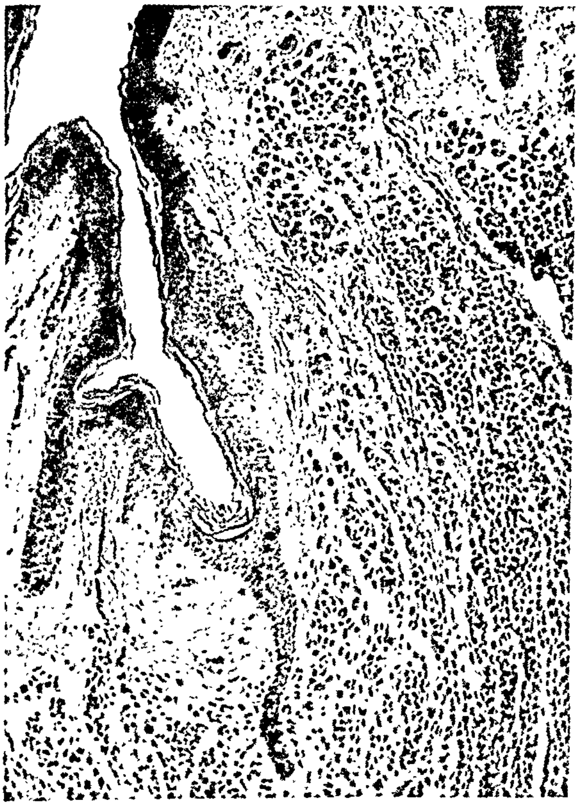

Fig. 4.—Low-power magnification illustrating arrangement of nevus cells into cords and clusters in superficial dermis.

In our opinion, there is but one safe and satisfactory means of removing these lesions, and that is complete surgical excision with use of the scalpel. Electrocautery, electrodesiccation, and radiation have been used in their treatment, but this is to be condemned. These agents all too frequently inadequately destroy the lesion, and thereby cause irritation which might be the stimulus to malignant transformation.

If possible, these lesions should be removed in childhood when the sensibilities of the patient have not been affected by his contact with the outside world. Performance of surgery at this age, as in McDowell's [2] case, results in better healing, lessened cosmetic disfigurement, and prevents degeneration and possibly malignant transformation of these tumors.

The question of removal of the lesion *in toto* or in stages will depend largely on the individual patient. Pack and Livingston[2A] express the belief that after puberty multiple-stage procedures should not be performed because of danger of malignant transformation. We agree with this theoretical premise, but feel that good surgical judgment will necessitate the removal of some of these lesions in stages.

Comment

Physical anomalies occasionally provide undesirable psychological reactions. The average person may have from 18 to 100 nevi, none of which causes undue apprehension, some of which may even be referred to as beauty marks; however, the giant nevus represents a stigma which causes its host to feel self-conscious and socially unacceptable, creating a profound distortion of his personality. It is appalling how frequent lesions which are remediable will be allowed to persist and progress to the point where they affect the person's mental equilibrium.

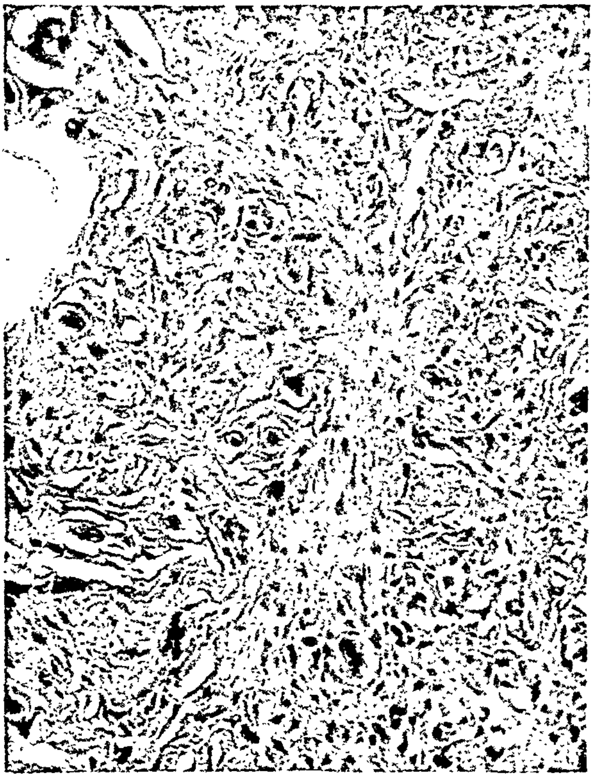

Fig. 5.—Low-power magnification of deeper portion of dermis and subcutaneous tissue. Note similarity to structure of neurofibroma.

Aside from its esthetic detraction and psychological sequelae, the malignant potentiality should be considered. Although it has been stated by some authorities that giant nevi never become malignant, evidence at hand seems to disprove this. Of the 53 cases which have been recorded in the lite
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CLINICAL NOTES

ADDUCTOR MUSCLE INJURIES IN BOWLERS

James R. Hoon, M.D., Sheboygan, Wis.

Bowling is considered a sport of little hazard and, as such, has not rated mention in recent articles on athletic injuries. Bowling injuries have usually been limited to fingers pinched in the ball rack and occasional toes bruised by dropped bowling balls. The cases here discussed concern another injury which can be related to the peculiar mechanics of bowling. The problem involves strain, and in one case actual avulsion, of the muscles of adduction of the thigh. Stress on these structures occurs during braking at the foul line on delivery of a bowling ball.

Report of Cases

Case 1.—A man, aged 44, weighing 220 lb. (99.9 kg.), 6 ft. (183 cm.) tall, with a heavy, protruding abdomen, sustained an injury to the right groin while bowling on Nov. 25, 1958. I observed the accident throughout its course, since I am a member of the patient's bowling team.

The patient, because of his formidable size, habitually delivered his ball while in a more erect position than the average bowler. On this occasion he threw the ball in an unusually powerful fashion, obtaining a resounding strike. He stopped firmly at the foul line in his erect position. In obvious severe pain, he then staggered and grasped the bowling ball rack in an effort to keep from falling. He paled and sweated profusely. He was placed in a reclining position, and in a few minutes the appearance of shock abated. Examination revealed an enlargement in the right inguinal region extending into the upper portion of the right side of the scrotum. The mass did not have the usual appearance of a hernia, since it lay somewhat posteriorly in the perineal region in addition to its extension into the scrotum. The mass was tender and not discolored, and the enlargement was not reducible by taxis. No previous swelling had been noted in this region by the patient. The initial diagnosis was probable incarcerated, acute, right inguinal hernia, with the posterior development of part of the mass noted as one unusual feature.

The patient was transported by ambulance to St. Nicholas Hospital, with no further attempts to stand or walk. He continued to have pain in the right groin and the medial aspect of the right thigh. On admission his blood pressure was 128/80 mm. Hg, pulse 88 per minute. The patient, having eaten a large supper, had his stomach evacuated by means of a Levin tube and suction. The pain remained marked. After consultation with his family physician (who was also bowling in the same league), the patient was admitted to surgery three hours after his injury.

Operation.—With the patient under general anesthesia, with intratracheal intubation and gastric suction, a right inguinal incision was made over the irreducible mass. The adipose panniculus was about 3 in. (7.6 cm.) in thickness. On exposure of the external oblique muscle dark, reddish-blue discoloration, apparently hematoma, was noted through the aponeurosis. This aponeurosis was divided, exposing the cord, which contained a large quantity of extravasated blood throughout its length. There was also a great amount of clotted blood in the inguinal canal and scrotum. No evidence of severe, active bleeding was present, however. Examination of the inguinal region revealed no sign of relaxation of the internal ring nor any hernial sac. The spermatic cord and testis were delivered into the wound. There were many large areas of hematoma throughout these structures.

Further exploration revealed a tear in the terminal floor of the inguinal canal at its entry into the scrotum. At this site disruption of the right adductor tendon (apparently mostly the adductor longus) at its origin from the front of the pubis was demonstrated. A splinter had been torn from the pubic bone along with this tendinous structure. From the relations demonstrable it appeared that the tearing of this bony structure across the posterior aspect of the cord had lacerated the vessels to the right testis, causing the bleeding into these tissues.

The degree of disruption of the blood supply to the testis and the amount of visible hematoma in the cord and testis made their removal mandatory. This was accomplished. Repair of the adductor tendon, reconstructing its insertion onto the pubic bone and further reinforcing the attachment by means of sutures to the adjacent adductor tendon group, was made. No further bleeding was noted. The defect in the floor of the inguinal canal and the operative opening in the external oblique muscle were then closed, and the subcutaneous tissue and skin were reunited without drainage.

Surgeon, the Sheboygan Clinic.

Read before the Wisconsin Surgical Society, Oshkosh, Wis., Sept. 19, 1959.

The question of removal of the lesion *in toto* or in stages will depend largely on the individual patient. Pack and Livingston[2A] express the belief that after puberty multiple-stage procedures should not be performed because of danger of malignant transformation. We agree with this theoretical premise, but feel that good surgical judgment will necessitate the removal of some of these lesions in stages.

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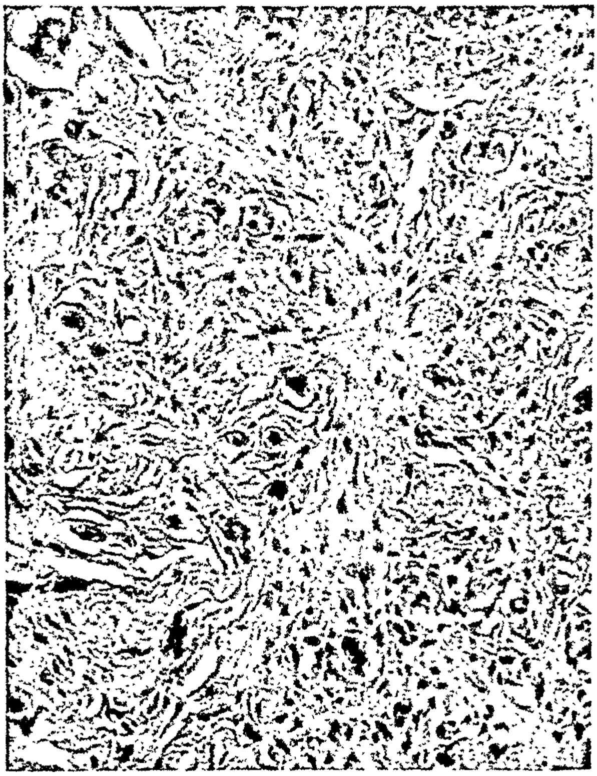

Fig. 5.—Low-power magnification of deeper portion of dermis and subcutaneous tissue. Note similarity to structure of neurofibroma.

Aside from its esthetic detraction and psychological sequelae, the malignant potentiality should be considered. Although it has been stated by some authorities that giant nevi never become malignant, evidence at hand seems to disprove this. Of the 53 cases which have been recorded in the literature 7[3] are known to have developed into a malignancy. This is a 13% incidence. Infection and chronic irritation appear to be the most common stimulus. When the question of malignancy in giant nevi arises, one must search its histogenesis for the answer. No matter which theory of origin of pigmented nevi one holds, the nervous or epithelial, it is a well-established fact that cellular nevi with junctional characteristics are more susceptible to neoplastic change. It has generally been assumed that most giant nevi are of the intradermal type, and are therefore unlikely to become malignant. Although this may be true in part, by virtue of the fact that the predominant histological characteristics of the lesions are intradermal, nevertheless, the existence of but one small zone of junctional *activity is sufficient evidence for the diagnosis of* a compound nevus. This case illustrates how easily one might have overlooked the single, small area of junctional activity (fig. 3) and arrived at an erroneous diagnosis of intradermal nevus. It is probable that in many cases of giant nevi areas of junctional activity go unrecognized because few sections are cut.

Another possible explanation for the misconception that all these lesions are solely intradermal is failure to realize that progressive changes occur in the histology of the nevus throughout its life. This was pointed out by Lund and Stobbe.[4] Proliferation at the junctional zone may occur either early or late in their natural history. When this change appears the nevus can no longer be classified as intradermal but must be considered a compound nevus, with its precancerous implication. We therefore conclude that all giant nevi are potentially malignant and should be removed when the patient is at an early age.

3636 St. Charles Ave. (15) (Dr. Reyes).

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The patient, because of his formidable size, habitually delivered his ball while in a more erect position than the average bowler. On this occasion he threw the ball in an unusually powerful fashion, obtaining a resounding strike. He stopped firmly at the foul line in his erect position. In obvious severe pain, he then staggered and grasped the bowling ball rack in an effort to keep from falling. He paled and sweated profusely. He was placed in a reclining position, and in a few minutes the appearance of shock abated. Examination revealed an enlargement in the right inguinal region extending into the upper portion of the right side of the scrotum. The mass did not have the usual appearance of a hernia, since it lay somewhat posteriorly in the perineal region in addition to its extension into the scrotum. The mass was tender and not discolored, and the enlargement was not reducible by taxis. No previous swelling had been noted in this region by the patient. The initial diagnosis was probable incarcerated, acute, right inguinal hernia, with the posterior development of part of the mass noted as one unusual feature.

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Operation.—With the patient under general anesthesia, with intratracheal intubation and gastric suction, a right inguinal incision was made over the irreducible mass. The adipose panniculus was about 3 in. (7.6 cm.) in thickness. On exposure of the external oblique muscle dark, reddish-blue discoloration, apparently hematoma, was noted through the aponeurosis. This aponeurosis was divided, exposing the cord, which contained a large quantity of extravasated blood throughout its length. There was also a great amount of clotted blood in the inguinal canal and scrotum. No evidence of severe, active bleeding was present, however. Examination of the inguinal region revealed no sign of relaxation of the internal ring nor any hernial sac. The spermatic cord and testis were delivered into the wound. There were many large areas of hematoma throughout these structures.

Further exploration revealed a tear in the terminal floor of the inguinal canal at its entry into the scrotum. At this site disruption of the right adductor tendon (apparently mostly the adductor longus) at its origin from the front of the pubis was demonstrated. A splinter had been torn from the pubic bone along with this tendinous structure. From the relations demonstrable it appeared that the tearing of this bony structure across the posterior aspect of the cord had lacerated the vessels to the right testis, causing the bleeding into these tissues.

The degree of disruption of the blood supply to the testis and the amount of visible hematoma in the cord and testis made their removal mandatory. This was accomplished. Repair of the adductor tendon, reconstructing its insertion onto the pubic bone and further reinforcing the attachment by means of sutures to the adjacent adductor tendon group, was made. No further bleeding was noted. The defect in the floor of the inguinal canal and the operative opening in the external oblique muscle were then closed, and the subcutaneous tissue and skin were reunited without drainage.

Surgeon, the Sheboygan Clinic.

Read before the Wisconsin Surgical Society, Oshkosh, Wis., Sept. 19, 1959.

The postoperative course of the patient was without disturbing incident. Early ambulation on crutches was possible, the patient being adjured against adducting and abducting his right leg. He was discharged from the hospital on crutches on the 12th postoperative day. On Dec. 17, 1958, evidence of hematoma of the inguinal region and scrotum had practically disappeared. Testing of adductors at this time demonstrated their integrity. The crutches were discarded on Dec. 24, 1958.

On Jan. 7, 1959, the patient walked well, with no demonstrable weakness of the right adductors. On Feb. 21, 1959, he engaged in his first postoperative bowling, with a score of 463 in a three-game series, including one game with a score of 192. This, he claims, compared satisfactorily with his preinjury state. On Feb. 25, 1959, at examination he had no discomfort and no apparent disability on walking, climbing and descending stairs, and engaging in his usual activities.

Case 2.—A man aged 45, a physician, 6 ft. 3 in. (190.6 cm.) tall, weighing 200 lb. (90.8 kg.), during the same bowling season sustained an obvious adductor strain. The patient experienced his injury by slipping, while attempting to deliver his bowling ball, when his left foot caught on a wet spot on the alley. This brought him violently to a halt. The patient described his distress as a sudden, whip-like pain from the leg throughout the body to his head, but concentrated in the left groin. Examination revealed no swelling or apparent disruption of structures but acute tenderness of the adductor gracilis region of the upper medial part of the thigh. The initial severe pain passed quickly, but discomfort in the left groin was of sufficient degree to prevent the patient from bowling for a period of about two weeks. Subsequently, he noted some dropping in his bowling score, as compared to preinjury levels, because of caution induced by his strain. The discomfort in the left groin persisted for four weeks.

Case 3.—A man aged 56, a dentist, of medium build, also experienced pain in the left groin on making a sudden balk at the foul line. His uncomfortable injury occurred in January, 1959. While examination revealed only tenderness in the region of the origin of the adductors and slight tenderness in the upper medial thigh, the patient's discomfort was of such degree that he avoided bowling for most of the remaining bowling season. No hematomas developed. By April, 1959, his discomfort had abated.

Case 4.—A man, aged 45, a city sanitation department employee, developed pain in the right upper medial thigh region on July 7, 1959, on lifting a large, heavy garbage can, overly filled, to his knee and then into the receiving port of his sanitation truck. The patient is slender but muscular. On the occasion of lifting the ungainly object he was forced to strain excessively to control it. He was examined a few hours after the incident. There was demonstrated no inguinal or femoral hernial impulse. The scrotum and contents appeared normal. The patient had almost exquisite tenderness over the upper course of the right adductor muscles, particularly the gracilis, became faint after gentle palpation of these muscles, and was forced to lie down for 10 minutes. No ecchymosis was evident. The diagnosis was strain of the right adductor femoris muscles. Treatment consisted of diathermy for two days and administration of analgesics. On July 10, 1959, there still remained moderate tenderness over the adductor region, but not of the exquisite nature earlier noted. There was a slight amount of induration apparent on palpation of the adductors on this day. He returned to work July 13, but because of pain in the upper medial thigh region he again ceased to work. Further diathermy treatment was then administered.

On July 21, 1959, he walked without a limp, although he still had slight tenderness on compression over the right adductor longus muscle. The discomfort had reduced sufficiently to permit the patient to return to work on July 22, 1959.

Comment

The case reports illustrate varying degrees of injury to the adductors of the thigh. Three concern injury incurred on suddenly stopping in a somewhat awkward position. The fourth occurred during an unexpectedly difficult lifting motion while hoisting a well-loaded garbage container onto a truck. They all involve strain, and in one case disruption, of the adductors, in each case of one thigh.

Strains are considered tearing of strands or fibers within a muscle, without complete division of the muscle itself. The injury may or may not be accompanied by external evidence of ecchymosis. The most severely injured patient (case 1) sustained disruption of the adductor longus at its origin and further injury, by laceration with a bone fragment, to the spermatic cord.

Adduction of the thigh is produced by several muscles, including the lower fibers of the gluteus maximus, but primary adduction is the function of the three adductor muscles, longus, magnus, and brevis, and the pectineus. In addition, the gracilis functions both as an internal rotator and an adductor. When the lower extremity is fixed, these muscles, taking their fixed points from the leg, act on the pelvis to help maintain the body in an erect position and, as in the cases here outlined, to prevent forward displacement of the body on an extended leg.

Another example of adductor action is grasping the sides of a saddle between the knees during riding. Christopher[1] mentioned a strain of the thighs, which he described simply as "rider's thigh." He may have thus been referring to another form of adductor strain.

Instances of complete disruption of a muscle or tendon are fairly common. Examples include (at the shoulder) ruptures of the supraspinatus and infraspinatus, the subscapularis tendon, and the long tendon of the biceps brachiae. Mathé[2] described an instance of traumatic avulsion of the psoas muscle which, by fibrosis, produced attacks of renal colic after three years. Disruption of the adductor longus muscle requires, as in these other disruptions, unusual force generally applied in an unnatural manner.

Prevention.—The importance of sound physical conditioning in the prevention of athletic injuries has frequently been emphasized. These injuries add emphasis to this basic principle. Case 2 resulted from an unexpected checking of motion at a wet spot on the alley. Cases 1 and 3 resulted from violent stopping efforts in an overly erect position at the foul line. These can be avoided by an altered approach to the foul line and by "following through" rather than braking violently. Case 4 involved the lifting of an unexpectedly heavy, large container, in an awkward manner, to the thigh and into a truck bed. The prevention of this, an industrial injury, concerns the use of proper lifting methods and of adequate assistance in lifting heavy objects.

Treatment.—Disruption of major tendon structures requires early, meticulous reconstruction and prolonged convalescent disuse. This was accomplished in case 1 by use of crutches and avoidance of adduction, abduction, and weight-bearing on the involved leg. Strains present a different treatment problem. Here early mobilization (avoiding excessive strain) is essential to avoid limiting fibroses and prolonged disability. Administration of analgesics and adjunctive physical therapy are helpful in achieving this early mobilization.

Conclusions

Four cases of injury to the adductor muscles of the thigh occurred; three in bowlers and the fourth in a public employee as a result of an industrial lifting accident. With disruption of the adductor longus, one of the bowlers required major surgical treatment. Prevention of such injuries entails proper conditioning and training.

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RENAL ARTERY ANEURYSM PRODUCING RENAL INFARCTION WITH RESULTANT HYPERTENSION

James B. Glanton, M.D., Robert L. Parsons, M.D.
and
Fred Mathers, M.D., Orlando, Fla.

A comprehensive review of the literature on true aneurysms of the renal artery reveals prior reporting of 142 cases. It is a rare pathological entity which occurs with a frequency of less than 0.015%[1]; in the case of renal infarction it has been reported as 1.4%.[2] The true incidence of hypertensive vascular disease in man is unknown, but the record of living subjects suggests that it is 24% or greater in the population ranging from the third to the seventh decade of life.[3]

A case report follows, in which an aneurysm of the renal artery was believed to have been responsible for infarction leading to renal hypertension. The hypertension was subsequently relieved by a nephrectomy.

Report of a Case

A 47-year-old man was seen as an outpatient on Dec. 30, 1955, complaining of severe right costovertebral angle pain, with radiation into the flank, of several days' duration. The patient also complained of severe headaches. Microscopic hematuria was found on several occasions.

The patient's history revealed that he had had a thrombosis of the veins of his left leg one year prior to the examination and had made an uneventful recovery. There was no other evidence of vascular disturbance and no familial history of renal disease.

Examination revealed the following significant findings. Blood pressure was 200/120 in the right and 210/120 mm. Hg in the left arm. Examination of the abdomen revealed tenderness to jarring percussion over the right costovertebral angle. Rectal

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From the departments of urology and medicine, Orange Memorial Hospital.

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examination was noncontributory. Intravenous urograms were done and found to represent normal findings bilaterally. Complete urinalysis revealed an albumin content of 3+ and an occasional red blood cell. The urine was centrifuged and many granular casts, both coarse and fine, were observed. Prior to this time there had been no knowledge that hypertension existed. The patient did not return for further evaluation but entered a veterans' hospital a few weeks later; during his hospital stay he experienced a recurrence of his right flank and right costovertebral angle pain, which persisted over a period of several days. After a few weeks he was discharged on a medical regimen for hypertension. His blood pressure remained elevated, however, and subsequently he was again observed and the possibility of renal infarction was considered.

The patient was admitted to the Orange Memorial Hospital in May, 1956, and the following day a lumbar aortogram was carried out which showed a decreased blood supply of the lower pole of the right kidney. The blood pressure readings while he was in hospital ranged from 192 to 150 mm. Hg systolic and 120 to 100 mm. Hg diastolic. A few days later, a right nephrectomy was carried out, with a preoperative diagnosis of right renal infarction. The renal artery was palpated and found to be markedly dilated, approximately 2 cm. in its greatest diameter just before its bifurcation. After further dissection it was realized that an aneurysm was present, and giving rise to the enlargement of the renal artery. Chromic ligatures were placed proximally to the aneurysm, and the kidney was removed without further difficulty. The preoperative blood pressure of 200/100 immediately dropped to 140/80 mm. Hg and remained such throughout the remainder of the procedure. The pathological report showed a kidney which weighed 150 Gm. There was 2 cm. of renal artery which, at the point of resection, showed an open sacular dilatation, about 1.5 cm. in diameter, which was partially lined by clots. No occlusion was noted in the renal artery or vein. There was a large depressed, sharply delineated scar occupying the posterior aspect of the kidney, measuring 6 by 5 cm. and extending across the midline to involve a small portion of the opposite half. This part of the kidney was a very dark red, and sections showed the dark red color to extend to a depth of about 0.7 cm.

Microscopic examination revealed extensive tubular atrophy in the scarred area, with resultant contraction of the glomeruli. In the medulla the tubules were moderately dilated and filled with hyaline casts. The pathological diagnosis was one of a large healing infarct of the right kidney and a sacular aneurysm of the right renal artery.

The patient was discharged on the eighth postoperative day and came for follow-up examinations in the office at six-month intervals, during which period his blood pressure remained normal. He was last seen in the office two and one-half years later, when his blood pressure was 122/90 mm. Hg. The patient has been rehabilitated in that his headaches have disappeared, his blood pressure has remained normotensive, and he has resumed his usual occupation since surgery.

Comment

The most frequent signs and symptoms of renal aneurysm are pain in 50% of patients, hematuria in 35%, palpable mass in 25%, hypertension in 15%, and bruit in 10%. Calcification in the wall of the aneurysm was found in only 25% of reported cases.[4] Sudden, persistent flank pain, associated with varying degrees of generalized collapse or shock, nausea and vomiting, and distention of the intestinal tract constitute the symptom complex of renal infarction.[2] The urine is often grossly bloody, although it may be clear initially. An adequate history helps to determine whether the infarction is arterial, venous, or traumatic. Diagnosis of a complete renal infarction is almost certain when excretory urograms show marked decrease or absence of function in the affected kidney and retrograde pyelograms reveal a normal collecting system and pelvis, without ureteral obstruction. Diagnosis in partial infarction, however, is difficult to make with intravenous urograms, as the reserve function in the unaffected portion of the kidney may fill the collecting system with sufficient contrast material to give a normal-appearing urogram.

In anyone with sudden onset of hypertension preceded by flank pain one should consider thrombosis or embolism of the renal artery. In any constriction of the renal artery the involved kidney will be smaller and softer. Unless contraindicated, all hypertensive patients should have intravenous urograms. The renal mass, even though reduced in size, may not always be demonstrable. The patient will also have a decrease in renal function, which may or may not be detectable.

In diagnosing renal hypertension cystoscopy and bilateral ureteral catheterization, with differential renal function studies, will be helpful. Another diagnostic aid is measurement of the urine volume and sodium concentration from each kidney. In ischemic kidneys, the urine volume and the sodium concentration are decreased; this was initially demonstrated in dogs by White[4A] a few years ago. Recently, Winter[5] used radioactive iodopyracet (Diodrast) compound in renograms, which method may provide a screening test of practical value. Renograms have also been performed by means of a radioactive tri-iodinated medium (Renograffin).[6] Previously, aortography had been used to confirm the diagnosis in questionable cases; at present, however, we are more reluctant to use this procedure because of reported adverse reactions.

Hypertension can be divided into two categories based on etiology,[1] which are (1) essential hypertension which has no known cause and (2) secondary hypertension which has a recognizable cause.

The diagnosis of essential hypertension is usually made by exclusion. Any sudden onset of severe hypertension should be considered of the secondary type until complete study reveals no known cause. Renal hypertension is the result of renal arterial lesions or due to parenchymal disease.

Histologically, one may predict the prognosis for hypertension in these unilaterally nephrectomized patients. A more satisfactory result is usually obtained in those patients whose kidneys pathologically reveal tubular atrophy, which is secondary to diminished blood flow. In those patients whose kidneys do not reveal the ischemic type of tubular atrophy, however, no benefit is obtained from the nephrectomy as far as relief from hypertension is concerned.[7]

Smith[3] has presented the case of unilateral renal disease in the hypertensive state very comprehensively. His study indicates that benign or accelerated hypertensive disease can be the result of unilateral renal disease and that it may be amenable to surgical correction. The incidence of successful nephrectomy for hypertensive disease has been estimated at 26%. However, if satisfactory results are to be obtained, the wise selection of cases amenable to surgical correction is important. The criteria considered necessary for a judicious selection[3] are (1) hypertension of less than two years' duration, (2) a persistent downhill course, (3) headaches and retinopathy (minimal changes), and (4) a diastolic blood pressure of 120 mm. Hg or more. Persistent lowering of blood pressure to 140/90 mm. Hg or lower for one year and alleviation of symptoms should be observed before a particular case is reported as cured.

Summary

In a case of true aneurysm of the renal artery, with subsequent infarction and hypertension, the latter condition was successfully relieved by nephrectomy. Although in this instance diagnosis was established by means of a lumbar aortogram, the performance of a renogram may provide a useful screening test, without the potentially adverse reactions recently ascribed to aortograms. If four major criteria are observed for a wise selection of cases, nephrectomy for hypertensive disease can be a successful procedure.

1321 Kuhl Ave., (Dr. Glanton).

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HEALTH CARE COSTS.—Abandonment of our system of private medicine and voluntary insurance for any government scheme could well be the straw that breaks the back of the American economy. Social Security benefits already promised, even if not further expanded in accordance with congressional election year custom, will require, by 1969, the collection of $216 per year from every worker earning $4800 per annum and a like sum from his employer. Today, for many, Social Security taxes exceed their income taxes. It is naive to assume that there is no limit to what government can exact from the citizen. Government creates no wealth. It can only take from one person and give to another while losing considerable of the nation's economic life-blood in the transfusion. Yet fully one-quarter of the 7300 bills now pending in Congress would confer special benefits on certain segments of the population without adequate provision for payment of these benefits. Enormous government spending even without the intensifying factor of recurrent deficits is the carcinogenic agent that triggers the cancer of inflation by increasing the cost of doing business at all levels while dampening economic incentives.—E. J. Faulkner, Chairman-Elect of the Health Insurance Council, Common Sense and Health Care Costs, *The Nebraska State Medical Journal,* August, 1959.

SPECIAL ARTICLE

PRESENT STATUS OF TREATMENT OF PERNICIOUS ANEMIA

NINTH ANNOUNCEMENT OF U. S. P. ANTI-ANEMIA PREPARATIONS ADVISORY BOARD

Frank H. Bethell,[†] M.D., Ann Arbor, Mich., William B. Castle, M.D., Boston,
C. Lockard Conley, M.D., Baltimore
and
Irving M. London, M.D., New York

The report in 1926 by Minot and Murphy[1] of the effectiveness of liver therapy in pernicious anemia soon was followed by the development of active concentrates of liver suitable for clinical use. By 1936 relatively purified extracts of liver were available for intramuscular injection, in addition to those preparations which earlier had been developed for oral administration. Owing to differences in animal sources and in manufacturing methods, the therapeutic effectiveness of these substances was not directly related to the amount of liver from which they were derived and could be estimated only by clinical tests of the final product.

Standardized Liver Concentrates

Standardization of preparations intended for the treatment of pernicious anemia was first prescribed by the *Eleventh Decennial Revision of the Pharmacopoeia of the United States* on June 1, 1936, as the responsibility of the Anti-Anemia Preparations Advisory Board.[2] In 1938, the Board defined as a U. S. P. unit that amount of a preparation which, when administered daily to patients with pernicious anemia, produced a satisfactory hematopoietic response. Since much more of a given liver preparation was required to produce therapeutic effects when administered by the oral route than when injected intramuscularly, the unit was further designated as either "oral" or "injectable," depending on the mode of administration. The Board was charged with the responsibility of reviewing and assessing confidential data submitted by pharmaceutical manufacturers pertaining to source of material, method of preparation and handling, packaging and labeling, and therapeutic effects of preparations intended for treatment of pernicious anemia. The assignment of units was based on the results of clinical assays employing three or more patients with pernicious anemia in relapse whose erythrocyte and reticulocyte responses were expected to approximate values obtained in previous experience with preparations known to be potent.[3]

Vitamin B_{12} in Liver Extracts

It was not until the isolation of vitamin B_{12} in 1948 that the identity of the anti-pernicious anemia principle of liver was established. Thereupon clinical trials soon provided convincing evidence that vitamin B_{12} is the principal, if not the sole, anti-pernicious anemia factor of purified liver extracts. When quantitative methods for measurement of the concentration of vitamin B_{12} became available, a study was conducted under the auspices of the U. S. P. to determine the vitamin B_{12} content of various preparations of liver for parenteral use to which U. S. P. units had been assigned. The results of this study showed that there was a considerable range of concentrations of vitamin B_{12} in preparations to which the same U. S. P. unitage had been assigned.[4] this was not a surprising finding, in view of the fact that clinical testing of consecutive lots manufactured by the same process was rarely possible, and because the variable responses obtained in different patients receiving the same preparation already had indicated the relatively crude nature of such clinical assays. Accordingly, in 1952, use of the U. S. P. unit (injectable) was discontinued, and the measure of activity of preparations intended for parenteral use became the vitamin B_{12} content of the preparations, as determined by official microbiological assay.[5]

More than a decade of experience now has amply confirmed the belief that parenterally administered vitamin B_{12} is as effective as injection of purified liver extract of equivalent vitamin B_{12} content, in the treatment of pernicious anemia. Patients who receive injections of appropriate amounts of vitamin B_{12} in either form at regular intervals remain in hematological remission and do not develop neurological or gastrointestinal manifestations of the disease. Vitamin B_{12} (cyanocobalamin, U. S. P.), a pure crystalline substance, is available in much higher concentration than in liver extracts, is nonirritating and nontoxic when injected, and is less expensive than in the form of liver preparations. For initial treatment of the patient in relapse, the dosage schedule employed is not a matter of great importance, since rapid clinical and hematological improvement appear to follow the injection of a single dose of about 30 mcg. Nevertheless, in order to restore the vitamin B_{12} concentration of depleted tissues, it seems wise to repeat the injection daily or several times a week, at least during the first week of therapy. An injection of as little as 30 mcg. of vitamin B_{12} given once each month is sufficient to maintain clinical and hematological remission indefinitely. However, it is now recognized that this amount is inadequate to restore the serum concentration of vitamin B_{12} to normal levels; therefore, larger maintenance doses are justified. The treatment of pernicious anemia with vitamin B_{12} given by the parenteral route thus is a sure and convenient therapeutic measure.

[†] Dr. Bethell, Chairman of the U. S. P. Anti-Anemia Preparations Advisory Board, died April 22, 1959.

On the other hand, the treatment of pernicious anemia with orally administered substances presents a complex problem. That effective therapy can be provided by the oral route was first demonstrated by Minot and Murphy.[1] However, it has long been known that much more is required of a given liver preparation when administered orally than when injected. Thus, hematological responses comparable to those following the daily injection of a U. S. P. unit of liver extract are usually produced by the daily injection of 1 mcg. of vitamin B_{12}. Some patients have had satisfactory responses to the oral administration of 25 mcg. of vitamin B_{12} per day; others have failed to respond to amounts as large as 250 mcg. per day. The reason for this now seems clear. Vitamin B_{12} is a large molecule which does not easily cross the intestinal mucosa. Normal persons appear to absorb little more of the vitamin from the usual mixed diet than the minute amount which is physiologically required, perhaps less than 1 mcg. per day. Absorption of even this small quantity is made possible by the presence in the normal gastrointestinal tract of "intrinsic factor," a substance produced by the gastric mucosa and apparently having the properties of a mucoprotein.

Intrinsic factor, by a mechanism which, at present, is not clearly understood, facilitates the absorption of vitamin B_{12}. The therapeutic use of the U. S. P. preparations powdered stomach, liver with stomach, or vitamin B_{12} with intrinsic factor concentrate depends, in each instance, on the activity of intrinsic factor in enhancing the absorption of the vitamin B_{12} in the product. However, the therapeutic effectiveness of mixtures of intrinsic factor and vitamin B_{12} cannot be estimated from the vitamin B_{12} content of the preparation. Although intrinsic factor concentrates of considerable potency have been prepared, the active agent has not been obtained as a pure substance and no simple laboratory test of established validity has been available by which its concentration and activity can be measured. Accordingly, to standardize preparations intended for the oral treatment of pernicious anemia, clinical trial is still essential, and it has been necessary to retain the U. S. P. unit (oral). In the assignment of units to such preparations the Board required that the final product of a specified manufacturing procedure, which contained the mixture of vitamin B_{12} and intrinsic factor to be marketed, be given to at least three patients with untreated pernicious anemia. In this way, numerous products containing liver and stomach or vitamin B_{12} and intrinsic factor concentrate have been demonstrated to produce satisfactory hematopoietic responses during clinical assays. Nevertheless, it cannot be inferred from these responses that all other patients with the disease will react as well.

Vitamin B_{12} Injections

Several considerations have led to the fear that oral administration of products to which U. S. P. units have been assigned may not always provide adequate treatment for patients with pernicious anemia. Certainly the amount of vitamin B_{12} that can be absorbed from the gastrointestinal tract, even from preparations containing intrinsic factor, is very small in comparison with the amounts which are readily injected parenterally. Intensive initial therapy cannot be provided with the preparations currently available for oral use. A single injection of 30 mcg. or more of vitamin B_{12} in patients with pernicious anemia in relapse is regularly followed by peak reticulocyte responses within five or six days. In contrast, when orally administered preparations are given at the usual dose of one U. S. P. unit daily, the peak of the reticulocyte response is usually delayed, often to about the 10th day. Moreover, in some patients with pernicious anemia, besides lack of intrinsic factor, defects of intestinal absorption may limit assimilation of vitamin B_{12}, especially when oral therapy is first begun.

Lifelong therapy with vitamin B_{12} is required in pernicious anemia, since the gastric lesion responsible for the deficit of intrinsic factor cannot be repaired. Recently a number of reports have appeared which indicate that some patients with pernicious anemia have experienced relapse while apparently receiving usual doses of vitamin B_{12} with intrinsic factor concentrate.[6] In some instances the patients had displayed initial satisfactory responses to treatment; but then, in spite of continued administration of the same preparation, anemia and other manifestations recurred. There is now good evidence that this is the result of an acquired refractoriness to certain intrinsic factor concentrates derived from animal sources. Tests with tracer doses of radioactive vitamin B_{12} have indicated that the intrinsic factor concentrates in question no longer appreciably enhance the absorption of vitamin B_{12} in these patients, although the same preparations are active in previously untreated patients. Development of such refractoriness has been observed within several months of the onset of oral therapy. In patients who had become unresponsive to such preparations, normal human gastric juice exerted its usual effect of potentiating absorption of vitamin B_{12}. Furthermore, in some instances other preparations of intrinsic factor from the same or different animal sources were effective. These observations have led to a series of investigations concerning the nature of the refractory state and the conditions under which it occurs. Some preparations seem to lead to the development of refractoriness more frequently than others, and quite possibly some do not have this action at all. At the present time, however, there is no means by which one can be assured that a product will not have this property for some patients. Preparations to which units have been assigned on the basis of the usual clinical assays thus may not be satisfactory for maintenance therapy of some patients with pernicious anemia. In the management of a disease for which parenteral therapy with vitamin B_{12} is a completely adequate and wholly reliable form of therapy, it is unwise to employ a type of treatment which is, at best, unpredictably effective.

Comment

The Sixteenth Revision of the U. S. P., which will become official late in 1960, will not include preparations intended for the treatment of pernicious anemia by oral administration. The U. S. P. unit will cease to exist, and the Anti-Anemia Preparations Advisory Board, having no further function, will be disbanded.

601 N. Broadway (5) (Dr. Conley).

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THE PREVENTION OF SCHIZOPHRENIA.—The gloomy view is sometimes taken, even by experts, that there can be little chance of preventing schizophrenia by public health measures when the hereditary forces seem so strong. This view is fallacious and can be refuted by pointing to the fact that twin-studies on tuberculosis show a genetic factor of precisely the same order as that shown by schizophrenia. To produce any disease, there must be a combination of genetic and environmental factors, and if the latter are sufficiently favorable then the disease will not develop, however strong the genetic loading. Rickets is another illustration of this, as Fraser Roberts has pointed out: 150 years ago it was considered hereditary; and so it is, in the sense that some people are genetically disposed to it and others genetically resistant. Yet once it was learned how to avoid the environmental factor (lack of Vitamin D) the disease became preventable and disappeared.—E. H. Hare, The Epidemiology of Mental Illness, *The Royal Society for the Promotion of Health Journal*, July-August, 1959.

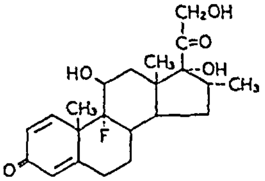
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the council.

H. D. Kautz, M.D., *Secretary.*

Dexamethasone (Decadron, Deronil, Gammacorten).—9α-Fluoro-16α-methylprednisolone.—The structural formula of dexamethasone may be represented as follows:



Actions and Uses.—Dexamethasone is a synthetic analogue of hydrocortisone, with similar actions and uses. It is the most potent anti-inflammatory gluco-corticoid yet available. Laboratory and clinical experience indicate that doses of 0.75 mg. of dexamethasone produce an anti-inflammatory response equivalent to that of about 4 mg. of triamcinolone or methylprednisolone, 5 mg. of prednisone or prednisolone, 20 mg. of hydrocortisone, and 25 mg. of cortisone. However, this greatly increased potency does not necessarily confer upon dexamethasone any special therapeutic advantage over other steroids with essentially the same pharmacological effects. Thus, except for using much smaller doses, therapy with dexamethasone may be expected to give results essentially the same as those anticipated with triamcinolone, methylprednisolone, prednisone, and prednisolone. As with the latter drugs, dexamethasone appears to lack the sodium-retaining and potassium-excreting properties of the earlier gluco-corticoids, cortisone and hydrocortisone. In fact, it may at first have a diuretic effect when substituted for cortisone or hydrocortisone in patients made edematous by these agents. In this respect, dexamethasone is well suited for long-term therapy in which steroid-induced fluid retention and electrolyte imbalance might otherwise become a problem. By the same token, the lack of mineralocorticoid activity with dexamethasone makes it inferior to cortisone, hydrocortisone, or fludrocortisone for replacement therapy in adrenal cortical insufficiency (Addison's disease). Hence, dexamethasone is used principally for its anti-inflammatory and antiallergic effects. It is useful in appropriate cases of rheumatoid arthritis and other collagen diseases, allergic conditions, inflammatory eye diseases, certain leukemias and lymphomas, soft tissue inflammations, hemolytic anemias, and other conditions generally considered responsive to systemic gluco-corticoid therapy. Some patients who respond poorly or are intolerant to other steroids may be managed satisfactorily with dexamethasone. As with all drugs of this class, the disadvantages and dangers, particularly since there is a tendency toward repeated use, should be weighed carefully against the benefit to be expected. Prolonged therapy with dexamethasone will suppress the function of the adrenal cortex; although ordinarily a hazard to its use, this property of the drug may be used advantageously in patients with adrenogenital syndrome.

Toxicity and Side-Effects.—Although clinical experience is not sufficient to permit quantitative comparisons, it is apparent that side-effects and untoward reactions to dexamethasone are qualitatively similar to those of other gluco-corticoids. It would appear from available data that dexamethasone has less tendency to cause salt and water retention and disturbance of glucose metabolism. The drug can cause peptic ulceration, decreased resistance to infection, demineralization of bone with resultant osteoporosis, insomnia, psychic disturbances, rounding of the face, fat deposition, hirsutism, acne, abdominal striae, petechiae, purpura, and amenorrhea. In common with all steroids, except triamcinolone which may cause decreased appetite and weight loss, dexamethasone causes an increase in appetite; weight gain may often be observed during prolonged therapy. The euphoria often seen with other steroids and the aggravation of the diabetic state have not been prominent with this drug. Relative contraindications to therapy with dexamethasone include active, latent, or questionably healed tuberculosis, other acute or chronic infections, peptic ulcer, osteoporosis, fresh intestinal anastomoses, diverticulitis, thrombophlebitis, and psychotic tendencies. Herpes simplex of the eye is an absolute contraindication except when the need for dexamethasone is considered greater than the risk to the function of the eye. The drug should be used cautiously in pregnant women, particularly during the first trimester, to avoid the possibility of postnatal hypoadrenalism in the fetus.

Dosage.—Dexamethasone is administered orally. Dosage must be individualized according to the severity of the disease, anticipated duration of steroid therapy, appearance of side-effects, and therapeutic response. In general, the total daily dosage of dexamethasone is about one-fifth that of triamcinolone or methylprednisolone and about one-sixth that of prednisone or prednisolone. In chronic conditions requiring long-term therapy, the lowest dose that will provide adequate, not necessarily complete, relief of symptoms should be used. This is because prolonged administration of high doses may produce unwanted hormonal effects. In life-threatening and other acute conditions, large doses are permissible and may be mandatory for short periods of time. The daily requirement is usually given in three or four divided doses. However, with the exception of acute conditions, administration of the daily requirement in two divided doses provides adequate therapy for some patients both initially and in maintenance.

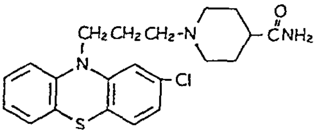
For rheumatoid arthritis, suppressive doses of 1.5 to 3 mg. per day may be given initially. Dosage is then decreased gradually to the smallest amount that gives the desired degree of symptomatic relief; this may be as low as 0.75 mg. per day. Alternatively, therapy may be initiated with small doses (0.75 to 1 mg. per day) and then increased gradually to eventual maintenance levels. For acute, nonfatal conditions such as seasonal asthma and self-limited ocular and dermatological disorders, daily dosages range between 2 and 3 mg. For chronic, potentially fatal diseases such as disseminated lupus erythematosus, pemphigus, and sarcoidosis, the usual initial dose is 2 to 4.5 mg. per day. For acute rheumatic fever, crisis of disseminated lupus erythematosus, and severe allergic reactions, initial doses of 7.5 to 10 mg. or more per day have been used. However, in such acute, life-threatening situations in which rapid onset of action is imperative, consideration should be given to the intravenous use of gluco-corticoids suitable for this route of administration. Massive doses of 10 to 15 mg. per day have been given to patients with acute leukemia, the nephrotic syndrome, and acute pemphigus. For the treatment of adrenogenital syndrome daily doses of 0.5 to 1.5 mg. are used.

Preparations.—tablets 0.5 mg. and 0.75 mg.

Year of introduction: 1958.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., and Schering Corporation cooperated by furnishing scientific data to aid in the evaluation of dexamethasone.

Pipamazine (Mornidine).—10-[3-(4-Carbamoylpiperidino)propyl]-2-chlorphenothiazine.—The structural formula of pipamazine may be represented as follows:



Actions and Uses.—Pipamazine is a substituted phenothiazine derivative with actions similar to those of other drugs of this chemical class. Thus, it exhibits both antiemetic and sedative actions. Pharmacological studies in animals indicate that, on a weight basis, pipamazine may be more potent than chlorpromazine in antiemetic activity but less potent in tranquilizing activity. Such studies suggest a relative specificity or increase in antiemetic action in relation to tranquilizing action. Hence, pipamazine is used clinically only for its antiemetic effects. The drug influences nausea and vomiting by an inhibitory action on the medullary chemoreceptor trigger zone; it does not act on the emetic center. After oral administration in human beings, the onset of action of pipamazine is about 30 minutes.

Pipamazine has been employed for the prevention and control of nausea and vomiting due to a variety of causes. These include emesis associated with pregnancy, anesthesia, radiation therapy, nitrogen mustard therapy, and gastroenteritis. In one controlled study, the drug reduced the incidence of vomiting after surgical anesthesia from 10% to 6%. The remainder of the clinical reports are largely uncontrolled. Nevertheless, it is the clinical impression of most observers that pipamazine is frequently effective for the symptomatic management of nausea and vomiting. Its ultimate usefulness in comparison with other antiemetic agents must await the results of additional controlled studies.

Toxicity and Side-Effects.—Doses greater than 10 mg. per day may, in occasional patients, cause mild to moderate sedation. With the exception of drowsiness, however, and, less frequently, postural hypotension, the usual therapeutic doses of pipamazine are well tolerated. Signs of extrapyramidal involvement (muscle spasm and Parkinson-like symptoms) have been encountered at dosage levels far beyond the usual therapeutic range. In occasional instances, abnormal values in certain liver function tests (serum bilirubin, serum transaminase, and sulfobromophthalein retention) have been observed, but overt jaundice or clinical signs or symptoms suggesting hepatic damage have not been attributed to therapy with the drug. Because it is a phenothiazine derivative, however, pipamazine should not be given to patients with known liver disease. For the same reason, it should be withheld in patients with leukopenia or other evidence of hematopoietic depression, even though there is no evidence that the drug depresses bone marrow function. Since it potentiates the action of other central nervous system depressants, caution is enjoined in the use of pipamazine in patients under the influence of narcotics, barbiturates, alcohol, or general anesthetics. Chronic administration in rats causes arrest of the estrous cycle in the progestational phase and reduction of weight of accessory reproductive organs in both sexes; the clinical significance of these laboratory findings is not known, but it might be important.

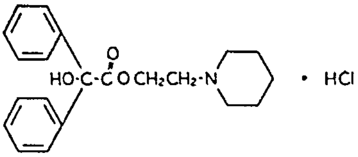
Dosage.—Pipamazine is administered orally or by intramuscular or intravenous injection. The usual dose for adults by the oral route is 5 mg. every four to six hours; if the drug cannot be retained orally, the same dose may be given intramuscularly. If intravenous administration is necessary, a dose of 5 mg. is injected slowly over a period of five minutes.

Preparations.—solution (injection) 5 mg. in 1 cc.; tablets 5 mg.

Year of introduction: 1959.

G. D. Searle & Co. cooperated by furnishing scientific data to aid in the evaluation of pipamazine.

Pipethanate Hydrochloride (Sycotrol).—2-(1-Piperidino) ethyl benzilate hydrochloride.—The structural formula of pipethanate hydrochloride may be represented as follows:



Actions and Uses.—Pipethanate hydrochloride, closely related in chemical structure to benactyzine hydrochloride, is proposed for use in the management of anxiety and tension accompanied by somatic complaints. It has been reported to be helpful in alleviating cardiac symptoms associated with anxiety, including palpitation, tachycardia, and angina; in the management of peptic ulcer, colitis, spastic colon, hypertension, coronary insufficiency, and menopausal complaints; and in ameliorating the tremors of senility and paralysis agitans. However, clinical experience with the drug is still extremely limited, and careful observations comparing it with other similar agents or with placebos have not been reported. Consequently, although favorable results have been described in the aforementioned conditions, further controlled clinical studies are required for convincing evidence that these results were attributable to the drug or that other drugs might not have given equally good or superior results.

In animals the drug has been shown to exert anticholinergic effects and to modify stress-induced behavior in a manner similar to that of benactyzine hydrochloride. It should be pointed out, however, that if the potency ratios observed in animals prevail in man, usual clinical doses of pipethanate hydrochloride would be expected to provide significantly less anticholinergic activity than customary doses of atropine and to influence behavior to a lesser degree than the usual doses of benactyzine hydrochloride. Pipethanate hydrochloride also possesses potent local anesthetic and quinidine-like atrial antifibrillatory actions, but these properties, demonstrated in the laboratory, have received no clinical application.

Although toxicity studies in animals are inadequate as reported, no undesirable effects, with the exception of drowsiness, have been reported in man. The possibility of serious systemic toxicity, however, has not been thoroughly explored either in animals or in human subjects. Therefore, patients receiving the drug should be carefully observed for untoward effects.

Dosage.—Pipethanate hydrochloride is administered orally. The proposed dose is 3 to 6 mg., three times daily.

Preparations.—tablets 3 mg.

Year of introduction: 1959.

Reed & Carnrick cooperated by furnishing scientific data to aid in the evaluation of pipethanate hydrochloride.

COUNCIL ON INDUSTRIAL HEALTH

The following statement, prepared by the Committee on Industrial Health Emergencies of the Council on Industrial Health, has been approved by the Board of Trustees of the American Medical Association.

B. Dixon Holland, M.D., *Secretary.*

GUIDE FOR INDUSTRIAL IMMUNIZATION PROGRAMS

Health maintenance is primarily the responsibility of the individual person; however, the employer has an obligation to provide a safe work environment for his employees, and he has a valid interest in the prevention of loss of work time and of work efficiency from his employees' ill health. Definitive diagnosis and therapy of nonoccupational injury or illness is not a responsibility of the employer; but he may provide certain preventive health measures in a given situation where the employee, the employer, and the community stand to benefit. While it is impossible to foresee every situation which might occur locally where an employer might properly make immunization procedures available to his employees, the following principles are offered as a guide.

1. Toward fulfillment of his obligation to provide a safe work environment, or to take appropriate precautionary measures, an employer should pro-

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Committee members are Norvin C. Kiefer, Ch., New York; Cortez F. Enloe Jr., New York; Allan J. Fleming, Wilmington, Del.; John N. Gallivan, East Hartford, Conn.; James H. Lade, Albany, N. Y.; Eugene Walsh, Chicago; and Lee N. Hames, Secretary, Chicago.

vide immunization procedures to employees who, by reason of their occupation or job assignment, may be exposed to significant hazards against which immunization procedures are available.

2. In keeping with his legitimate right to operate efficiently and profitably in a free enterprise system, with his responsibility to the community, and in demonstration of his good corporate citizenship and concern over his employees' health, an employer may provide immunization procedures in the face of an impending epidemic which threatens to disable so large a proportion of his employees as to interfere materially with operations and against which immunization procedures could not be applied by community health resources in a short enough period of time to afford the optimum protection. The component medical society's approval of company immunization programs conducted under these circumstances should be sought, and to the extent feasible and practicable local physicians should be afforded an opportunity to participate in them.

3. Additionally, an employer may wish to participate in community-wide immunization programs at the request of and in cooperation with a local medical society and community health agencies.

COMMITTEE ON REHABILITATION

The following report is the fourth in a series of articles which have been authorized for publication by the Committee. The first three appeared in The Journal *on Oct. 24, Nov. 7, and Nov. 21, 1959, pp. 1107, 1359, and 1694. This series deals with various aspects of rehabilitation which are of interest to physicians.* Ralph E. De Forest, M.D., *Secretary.*

PSYCHIATRIC REHABILITATION

Benjamin Simon, M.D., Arlington Heights, Mass.

World War II marked the beginning of modern psychiatric rehabilitation as we know it today. Occupational therapy had served, almost alone for a century, to supply the need of the psychiatric patient for normal activity and as a means of teaching him some avocation which he could take home as a therapeutic hobby. Other activities such as sports, movies, and music were added in an occasional and unorganized fashion. By default, these activities often came under the direction of the occupational therapist who was the one person with a formal training in paramedical activities and who was recognized as a qualified technician.

With the extensive application of group psychotherapy came the awareness of problems besetting military psychiatric patients—problems involving attitudes toward illness, attitudes of the self to illness and to the attitudes of others, problems of self-esteem, problems of adjustment within the hospital, and problems of adjustment outside the hospital. These concerns were personal, social, and economic; they included problems of relationships with parents, spouse, the Army, the community, and employers.

The special character of the psychiatric patient brought these problems out in much stronger relief. Generally, the patients were not confined to bed or suffering from a physical disorder around which their interest centered. On the surface they were not ill. Usually, they were fully ambulatory, with only a small portion of their time and interest devoted to medical treatment, including psychotherapy. The very nature of their emotional disorders involved an enlarged caricature of the general problems of the "normal" medical patient.[1] The rest of the patient's hospitalized time was an empty void, a small portion of which was filled in by occupational therapy. In contrast to the ordinary state hospital filled with psychotic patients with the accompanying management problems, many patients in the Army hospital were not psychotic and were capable of being handled like "normal" persons, as indeed were most of the psychotic patients as well, particularly when under psychiatric treatment.

The major problem in the care of psychiatric disorders seemed then to divide itself into two ill-defined segments: (1) the programming of activities within the hospital and (2) planning for the future and programming in this direction. The ultimate outcome of serious application to these problems was the development of the reconditioning programs including physical activities, handicraft activities, educational activities, music activities, recreational activities, and others as they developed. The continuous scrutiny of these activities which came up in group therapy sessions

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Chairman, Committee on Rehabilitation, American Psychiatric Association.

served eventually to develop the general principles of rehabilitation which the Army called "reconditioning."

Psychiatric rehabilitation has been variously defined, and opinions still differ. In the "American Illustrated Medical Dictionary"[2] it is defined as "The restoration to useful activity of individuals who have been wounded so as to suffer from physical or emotional disability, such restoration including treatment of the disability and training to fit the individual for occupation in industry." Other dictionary definitions place even more emphasis on restoration to economic productivity. The Commission on Chronic Illness[3] defines rehabilitation as "The restoration of the handicapped to the fullest physical, mental, social, vocational, and economic usefulness of which they are capable." The range of services was classified into three principal areas: (1) medical–medical and psychiatric diagnosis and treatment, together with such supportive services as physical therapy, occupational therapy, speech therapy, and nursing care; (2) psychosocial–social and psychological evaluation, social casework, and personal counseling; and (3) vocational–prevocational evaluation and experience, vocational counseling, graduated physical preparation and hardening, vocational training, trial or permanent employment in a sheltered workshop, and selective placement in employment.

Some have quarreled with these definitions and have felt that they did not include, for example, the work with mentally retarded or chronic mental patients who had never attained a reasonable level of social adjustment prior to the illness. It would seem that, while the term "habilitation" might be applicable to these, there is no real need to be so specious if we consider that the object is to attain the fullest adjustment of which any person is capable.

Therapeutic Use of the Self

The concept of the "therapeutic use of the self" applies to all persons (including physicians) who stand in a professional relationship to mental patients, even though such persons may not be practicing psychiatry in its restricted sense. The Committee on Psychiatric Nursing of the Group for the Advancement of Psychiatry crystallized this idea in the article "Therapeutic Use of the Self—A Concept for Teaching Patient Care."[4] The introduction to the article sets forth useful and important guiding principles which, when paraphrased, call for the following things: (1) an understanding of the behavior of the mentally ill patient and an appropriate response to it by all personnel to assure effectiveness in the day-by-day care of the patient; (2) a better recognition of the patient's emotional needs, awareness, and the use by personnel of supporting and corrective responses to his emotional needs, including an appreciation of some aspects of interaction between patient and nurse and its meaning and application in the therapeutic effort; (3) the hospital to serve as a smaller, limited world wherein new experiences in living and new personal relationships produce minimal anxiety and maximal support so that the patient gradually may be helped to feel that living with others is less threatening and a less forbidding experience. This is necessary since a patient enters a psychiatric hospital because he has experienced difficulties in living in the outside world. Whatever the nature and expression of these difficulties, they invariably include a breakdown in relationship with other people; (4) a hospital program which enables the patient to learn to live more effectively with other people. Every mental illness includes the problem of the patient's particular way of relating himself to others and of participating with others in activities. When a patient enters a mental hospital, he has already established patterns of behavior intended to facilitate his withdrawal from anxiety-provoking relationships. Withdrawal may be variously expressed. In the attempt to cope with his anxiety, the patient chooses that form of expression which, in his experience, has been most effective in maintaining distance from others for his subjective comfort; (5) personal relationships which gratify the patient's needs, facilitate his communication with others, and enhance his social participation. If these relationships remain essentially therapeutic, the patient-personnel relationship can become an integral part of the whole therapeutic regimen. It is important for personnel to understand and to be aware of the feelings, thoughts, and actions of the patients. They should have a similar understanding of their own thoughts and actions in any situation. Such awareness is acquired gradually and depends upon collaboration with the psychiatrist, conferences with supervisors and co-workers, and repeated experiences with patients.

Although these principles were originally intended for "nursing personnel," it became quite apparent that this philosophy of patient care extended through all the areas in which patients were related to personnel and that this was especially applicable to personnel in the so-called rehabilitation services.

The Psychiatric Hospital, the Community, and the Patient

There has been a very strong shift from concern with the activity, or modality, to the psychodynamics of the personal relationship. Emphasis is now predominantly on the needs of the patient as a whole person; the modality used has become the focus about which the relationship may develop and progress. This has significantly changed the conception of the psychiatric hospital which is now becoming the "open hospital" and the "therapeutic community."[5] The "open hospital" repeatedly underscored the increasing need for patient activities and relationship with personnel in all categories. Architectural planning for hospitals also had to be reconsidered in the light of this new approach to rehabilitation. These aspects have been discussed by Martin,[6] Simon,[7] and others.

The Patient's Adaptation

Rehabilitation today clearly includes every aspect of the treatment of the whole person. This is pictured by Greenblatt [8] (fig. 1) as a function of the individual's adaptation to six essential areas of living: psychological, vocational, family, sociorecreational, educational, and community. Throughout life, the patient tries to increase his "life space" against internal or external resistance. Success in all areas is represented, diagrammatically, in terms of an equilateral hexagon. In terms of this model, deficiencies or imbalance in any given area can produce a variety of asymmetrical hexagons.

The disturbance in the symmetry of the rehabilitation "life space" of course will antedate hospitalization and will determine the type of help which the patient must have in the various areas of living.

In the attempts to solve the many difficulties in readaptation of the patient to the community, many modifications in hospital organization and procedure developed. One of the earliest was the Family Care Program. Historically, the earliest was the famous Gheel Colony, the prototype of the family care program of the state hospital. There is now a large number of agencies and programs designed to implement the transitional phase of the patient's return to the community, where he cannot return directly. The impact of rehabilitation in the newer sense has resulted in the establishment of such transitional agencies and institutions as the Altro Rehabilitation Centers, halfway houses like Portals and the Vermont Center,[6b] social-therapeutic clubs like Fountain House, after-care clinics, and changes in the hospital, giving it a more participant role in the community life of the patient. The day and night hospitals are examples of this.

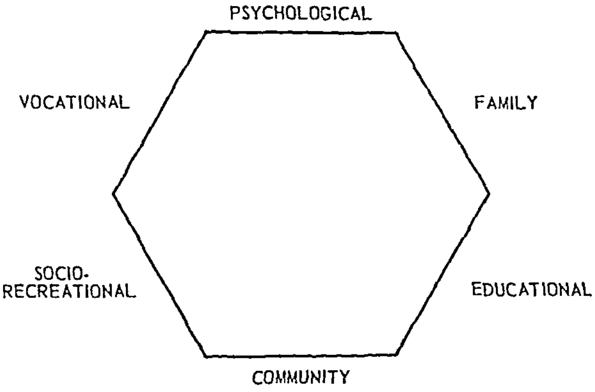

Fig. 1.—The rehabilitation "life space."

Greenblatt [8] pictured the transitional steps of the patient's return to the community from the hospital in a staircase (fig. 2), which includes all available resources in which, as an individual, each patient follows his own pattern. No given order of steps could be considered as satisfactory for all patients.

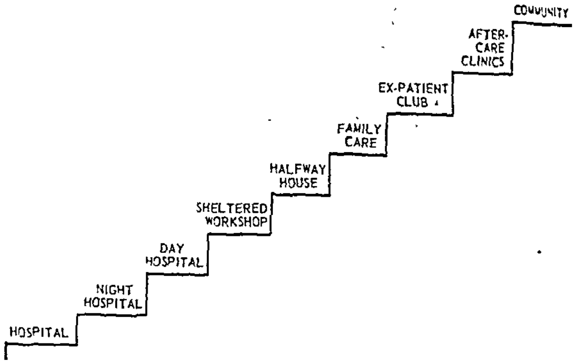

Fig. 2.—Transitional steps in patient's return to community.

The Hospital and Community

As one surveys this movement of patients, it is apparent that there is a continuum of movement, not only from the hospital to the community but from the community to the hospital. These various rehabilitation facilities and agencies may play a role in the prevention of hospitalization as a stage short of hospitalization to which the patient may temporarily regress for further help in continuing in the community. From this point of view, then, the hospital program and the community are integrated into one, with a continuum of psychiatric service going "upstairs" or "downstairs," as may be necessary. Clearly, the leadership should lie with the medical staff in the hospital, and it should play an important role in the organization and direction of the total program. The hospital service now truly fulfills its role as stated earlier—both as an extension of the community and as a model of the community—the "open hospital" and the "therapeutic community." In a similar sense, the community becomes a model of the ideal hospital and, through its agencies, performs for those of its citizens who need it the functions of the many rehabilitation divisions of the hospital itself. It is clear that the rehabilitation of the patient now really begins before his hospitalization, and therapy and practice should be under way in the hospital without delay. No longer is it a procedure to be employed when the patient is "ready to go home." The boundaries between home, community, and hospital have blurred.

Of ever-increasing importance will be the role of the family physician in the community as the "medical" part of the community program. To this end, there has been an increasing number of seminars and classes for general practitioners, in addition to development of closer relationship between hospitals and physicians in the community.[8]

Homemaker services to care for the family of a patient during the period of hospitalization, in close coordination with the care of the patient, have become increasingly effective.[9]

In the same manner in which the community physician is becoming an extension of the hospital in the community, so the hospital physician is being encouraged now to be an active member of the community without the hospital as well—to the end that the mental hospital of today and in the future will be truly a community mental hospital.

Summary

The concept of rehabilitation of the psychiatric patient in the last decade has extended far beyond the simple dictionary definition of the term. The four major trends which stand out today are (1) the "open hospital" and the "therapeutic community," which have created the need for the great increase in rehabilitation services, the increased close relationship of the hospital with the community, and the establishment of the hospital as an integral part of the community; (2) the application of psychodynamics embodied in the "therapeutic use of the self"; (3) the development of a great variety of transitional agencies between community and hospital for the implementation of a program built around the person as a psychological whole. The need for integration and direction of the total program in the interests of the whole person is apparent. If these programs are developed, the need for education and training of both professional personnel and nonprofessional volunteer personnel becomes apparent. The need for good organization and coordination is obvious. This is true not only within the hospital setting, where there is a growing category of rehabilitation coordinators (coordinators of adjunctive therapies),[10] but in the coordination of community activities as well. In this respect, the community physicians will play an important role both in the coordination of activities and in direct assistance to the various rehabilitation units and organizations; and (4) the establishment of the mental hospital as a true "community hospital" with an "open door" through which hospital personnel, from the medical staff on, are encouraged to make themselves a part of the community and through which the physicians of the community, psychiatrists and nonpsychiatrists, are encouraged to make themselves a part of the hospital.[11]

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TRANSMISSION OF INFECTIOUS HEPATITIS.—Since the nineteenth century there have been epidemics of jaundice that have been attributed to water-borne transmission. The evidence accumulated in recent years is sufficiently complete to warrant recognition of this mode of spread of infectious hepatitis as an epidemiologic entity. In this regard, infectious hepatitis is the first viral disease for which a water-borne route of infection has been generally accepted. Such a route has been postulated for poliomyelitis, but no studies have been reported in which conclusive evidence was obtained. It is believed that person-to-person contact is the most frequent type of transmission of infectious hepatitis and there is no evidence to the contrary at the present time. It is important to recognize, however, that it is difficult to establish the water-borne route of infection, and it may account for more cases than can be demonstrated by available methods.—J. W. Mosley, M.D., Water-Borne Infectious Hepatitis, *The New England Journal of Medicine,* Oct. 1, 1959.

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YOUNG TURKS—OLD TURKS

IT IS gratifying to discover that sophistication in clinical investigation, which is almost synonymous with academic medicine, does not necessarily scorn the romantic. At least the emotional tropism that draws us to an institution or to an organization may be powerful enough to counteract any stigma of sentimentalism when one is assigned the honor of assembling the chronicles of such an organization, so that the present will not forget the past. In a recent issue of the *Journal of Clinical Investigation* (special issue, 38:1783-1878, Oct. [pt. 2] 1959), a special supplement edited by Ellen R. Brainard was devoted exclusively to a recounting of significant events in the formation, early days of struggle, and rapid development of a coterie of clinical investigators into a community of scholars known as the American Society for Clinical Investigation—the Young Turks.

The person responsible for the idea was Dr. Samuel J. Meltzer, Russian-born and German-trained, a transatlantic ship's doctor until he was attracted permanently to the United States in 1883. At the age of 53 he abandoned a lucrative practice of medicine in Harlem to become associated with the newly established Rockefeller Institute for Medical Research. For some time the eponym for the American Society for Clinical Investigation was the Meltzer Verein, in honor of this distinguished scientist and in deference to his Teutonic training. According to the best recollection, the idea for the society was founded on the boardwalk in Atlantic City, after a session of the American Medical Association in 1907. The first meeting of the society occurred two years later. The members were identified as Young Turks to emphasize the revolt against the Association of American Physicians, the Old Turks. The prevailing sentiment in the founding of the American Society for Clinical Investigation was the unwritten pledge to foster the evolution of the young investigators into wise professors of our medical faculties. Just 15 years after the society was founded the first issue of their periodical, the *Journal of Clinical Investigation*, was published.

Concomitant with the compilations of the history of the Young Turks, two Old Turks in formal academic, but not intellectual, retirement have been laboring to bring up-to-date the records for their respective corporate structures. Dr. J. Howard Means, one-time Jackson professor of medicine at Harvard Medical School, one-time member of the editorial board of the *A. M. A. Archives of Internal Medicine*, and one-time president of the Association of American Physicians, is preparing the history of the association during its 75 years of growth. Also, Dr. C. Sidney Burwell, one-time dean of Harvard Medical School and one-time professor of research medicine at Harvard, is compiling a history of this institution of learning for the first half of the current century. It is suspected that there will be considerable overlapping in persons and projects in these three significant documents.

The American Society for Clinical Investigation has a composition of about 275 active members. Many of the Young Turks in the original roster remained in clinical investigation and, by the time their turn came for graduation to Old Turks, were elected to membership in the Association of American Physicians. The current panel of emeritus members of the society contains the names of almost 500 physicians and medical scientists. Last, the history of the society lists almost 150 Old Turks who have joined their patients. Whether active, emeritus, or in the third category whose activity remains unknown, the vast majority have been dedicated to research, the pursuit of clinical investigation, and the teaching of the art as well as the science of medicine to pregraduate and to postgraduate disciples.

To paraphrase A. Lincoln, the world will soon forget what is said here but it will long remember what they did here. There are several Nobel laureates on the registry of the society. The deans of medical schools are as abundant as the seeds in a watermelon, while the number of professors in medical schools are as "thick as autumnal leaves that strow the brooks in Vallombrosa." Whether one looks kindly or not on those who pursue investigation and are dedicated simultaneously to bedside teaching, this conclusion seems inescapable: The inventory of Young Turks and Old Turks is intrinsic to the tremendous progress in the art and practice of medicine in America since the beginning of this century. The history of the Society of Clinical Investigation is an intriguing document. We await with anticipation a similar volume of the Society of Old Turks as well as the history of the last half-century of the Harvard Medical School, where so many teachers of medicine received a modicum or a significant portion of their formal professional education.

BIOCHEMICAL ASPECTS OF ERYTHROCYTE FORMATION

The mature erythrocyte consists of about 90% hemoglobin by dry weight; the remainder is stroma and an impressive array of enzymes. Some of these enzymes are concerned with oxygen and carbon dioxide transport while others may be vestiges of previous existence as a cell capable of division. Recent investigations have contributed to the understanding of the mechanisms involved in biosynthesis of various components of the red blood cell. Interest has been focused principally on the manner of hemoglobin synthesis.

Understanding of the biochemistry of heme synthesis had its inception in the discovery of Shemin and Rittenberg[1] that glycine labeled with isotopic nitrogen (N^{15}) administered to animals gives rise to erythrocyte heme containing N^{15}. With this observation as the foundation almost the entire biosynthetic pathway of heme has been elucidated. Rapid advances in this field followed quickly upon the finding by Shemin and his colleagues[2] and by investigators in England that heme synthesis could be studied in vitro with use of avian erythrocytes, reticulocytes, or hemolyzates of these cells. The well-documented sequence of reactions by which heme is formed is as follows.

Glycine condenses with an activated succinate derivative (probably succinyl coenzyme A), to yield α-amino-β-keto adipic acid which either enzymatically or spontaneously loses a carboxyl group to become δ-amino levulinic acid. Two molecules of δ-amino levulinic acid condense to form the pyrrole, porphobilinogen. The enzyme carrying out this condensation appears to be a copper-containing, sulfhydryl enzyme. The detailed mechanism of how four phorphobilinogen molecules condense, lose six carboxyl groups, and form two double bonds in the side chains resulting in protoporphyrin is still not clear. It seems probable that uroporphyrin and coproporphyrin (containing eight and six carboxyl groups, respectively) are not direct precursors but are formed from intermediates which also yield protoporphyrin. The more direct precursors may be the porphyrinogens, i. e., the reduced forms of the porphyrins.

There is still doubt concerning the step at which the iron is incorporated into the molecule. Experiments with chicken erythrocyte hemolyzates have shown the possibility of an enzymic reaction between ferrous iron and protoporphyrin to yield heme. This reaction also occurs nonenzymically. Evidence derived from experiments with liver mitochondria substantiates the enzymic pathway. It is not certain whether the iron is derived from ferritin or directly from transferrin (siderophilin). The mechanism of reduction of the ferric to the ferrous form needs to be clarified.

The other part of the hemoglobin molecule, globin, has been the subject of intensive study[3] as one example of protein synthesis. It appears likely that globin is formed by the same type of reaction sequence as are other proteins. The process by which globin is linked to heme is uncertain, although model experiments have shown that analogous reactions occur spontaneously.

Under normal conditions the formation of globin and of heme keep pace with each other so that no accumulation occurs of either excess porphyrin or protein. The mechanism of this fine degree of regulation poses an interesting, important, and as yet unsolved problem.

The biochemical role of cyanocobalamine (vitamine B_{12}), which has such a striking effect in restoring normal maturation of erythroid cells in pernicious anemia, has not been established. Since vitamins, at least those whose chemical functions are understood, are constituents of coenzymes, attempts have been made to find a coenzymic role for this vitamin. Reports have appeared of the participation of cyanocobalamine in reactions involving deoxyriboside formation, incorporation of amino acids into proteins, reduction of the hydroxymethyl group of serine and transfer to homocystine to form methionine, and in the formation of the methyl group of thymine. None of these reactions accounts for the high degree of specificity of the maturation arrest characteristic of pernicious anemia and the dramatic release of this maturation arrest by minute amounts of the vitamin.

In the last few years evidence has accumulated which firmly establishes the hypothesis of Carnot[4] indicating the existence of a hormone which regulates erythropoiesis. This factor, erythropoietin (hematopoietin, hemopoietine) appears in small amounts in normal blood and in elevated amounts in response to either anemic anoxia or anoxic anoxia in many species, including man. The administration of cobaltous chloride to experimental animals also results in increased plasma titers of erythropoietin. This finding probably explains the polycythemia-producing effect of cobalt. While it has not yet been completely purified, this hormone is apparently a glycoprotein. It is relatively heat and acid stable but is inactivated by proteolytic enzymes.

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There is evidence indicating that in the experimental animal erythropoietin is formed in the kidney. Such an origin for erythropoietin may serve to explain the anemias associated with renal disease and the polycythemia sometimes present in conjunction with hypernephroma. There have been no reports of the use of erythropoietin in the treatment of anemias in man.

SMOKING AND LUNG CANCER

A summary of pertinent data relating to smoking and lung cancer appeared in The Journal, Nov. 28, pages 1829 to 1837. Written by Dr. Leroy E. Burney, surgeon general of the Public Health Service, the report documents the major researches and identifies the Public Health Service with those who consider that the evidence to date implicates smoking as the principal etiological factor in the increase in lung cancer. A number of authorities who have examined the same evidence cited by Dr. Burney do not agree with his conclusions. Although the studies reveal a relationship between cigarette smoking and cancer that seems more than coincidental, they do not explain why, even when smoking patterns are the same, case rates are higher among men than among women and among urban than among rural populations. Neither the proponents nor the opponents of the smoking theory have sufficient evidence to warrant the assumption of an all-or-none authoritative position. Until definitive studies are forthcoming, the physician can fulfill his responsibility by watching the situation closely, keeping courant of the facts, and advising his patients on the basis of his appraisal of those facts. The Public Health Service can best meet its obligations by collecting and disseminating data from all sources and making known to the health and medical professions its own evaluations of such data.

J. H. T.

MEDICAL FILM REVIEWS

Circulation of the Blood: 16 mm., color, sound, showing time 7 minutes. Produced in 1958 by Churchill Wexler Film Productions, Los Angeles. Procurable on loan or purchase from American Heart Association Film Library, 267 W. 25th St., New York 1.

This film, by means of diagrammatic drawings, shows how the heart works and explains the structure of the arteries and how their expansion and contraction controls the flow of blood. Animated diagrams trace the circulation of the blood through the body. This is a stylized, accurate, and attractive presentation of the activity of the normal human heart. The animated diagrams are augmented by a few actual views of the movement of blood in capillaries, arterioles, and venules, and the animation and narration are excellent. The film is highly recommended for adult lay groups and also for supplementary material in college and high school classes in biology, physiology, and health education.

Physical Examination of the Newborn: The Art and the Findings: 16 mm., color, sound, showing time 33 minutes. Prepared by Mary B. Olney, M.D., San Francisco. Produced in 1959 by Medical Arts Productions, San Francisco for and procurable on loan from Pfizer Laboratories, 630 Flushing Ave., Brooklyn 6, N. Y.

Part 1 of this film demonstrates the steps of a complete routine examination as it is performed on a baby a few hours old. Part 2 shows special examination techniques and some of the more common abnormal findings as well as normal findings which can be mistaken for anomalies. One of the best parts of this film is the last sequence, in which the pediatrician visits the mother with the newborn infant and demonstrates to her many of the points in the physiology of newborn infants which might possibly disturb her. This is a very good illustration of putting a mother at ease with her newborn baby. This film is an excellent demonstration of physical examination of newborn infants and it is highly recommended for obstetricians, pediatricians, general practitioners, and house officers.

The Thiersch Wiring For Massive Rectal Prolapse: 16 mm., color, sound, showing time 15 minutes. Prepared in 1958 by and procurable on loan from Robert Turell, M.D., 25 E. 83rd St., New York 28.

This film demonstrates the technique of inserting a Thiersch wire for the control of rectal prolapse. The author's indications for using this procedure, as well as his program of preoperative and postoperative care, are described. Photographs demonstrate the condition of patients before and after the operation and roentgenograms are shown of the wires in place after surgery. Some of the complications of this operation are described; however, a rather common one, fecal impaction, has been omitted. The technical details are well presented, but one must look at the indications for this procedure with a very critical eye. The photography is good and the film will be of interest to proctologists.

MEDICAL NEWS

ARKANSAS

Student Building Dedicated.—The Jeff Banks Student Union Building at the University of Arkansas Medical Center, Little Rock, was dedicated Nov. 20 to the memory of the late Dr. Jeff Banks, former head of the School of Medicine anatomy department. The ceremony also officially opened the medical center's new Residence Hall which has been occupied by students since the start of the 1959-1960 school term. Construction on the two buildings, financed by the federal government, was completed this summer. The Residence Hall is a 10-story facility to accommodate 315 single students and 95 married couples in efficiency apartments. The Student Union contains the main lounge, coffee shop, recreation room, barbershop, music room, and administrative offices. Dr. James D. Mashburn, of Fayetteville, responded to the dedication for the Jeff Banks Memorial Student Aid Fund. The fund was started to help finance the education of needy and deserving students in the School of Medicine.

CONNECTICUT

Visiting Professors.—Dr. William C. Gibson, Kinsman Professor of Neurological Research at the University of British Columbia, will be visiting professor of the history of medicine at the Yale University School of Medicine, New Haven. Dr. Horst Bickel was appointed visiting associate professor of pediatrics at Yale from August to November. He has been assistant professor at the University Children's Hospital, Marburg an der Lahn, Germany, since 1954. Dr. Bickel is participating in the teaching activities of the department of pediatrics and continuing his research in inborn errors of metabolism. During the current academic year, Noah Lichtenstein, Dr. Phil., will serve as a visiting associate professor of biochemistry. Since 1954, he has been associate professor of biochemistry at the Hebrew University in Jerusalem. While at Yale, he will participate in graduate seminars and teaching of the first-year medical students.

ILLINOIS

Clinics for Crippled Children.—Clinics for physically handicapped children in Illinois have been scheduled by the University of Illinois, Division of Services for Crippled Children. Fifteen general clinics were scheduled for December providing diagnostic orthopedic, speech, and hearing examination along with medical, social, and nursing service. Any physician may refer to a convenient clinic any child for whom he may want examination or consultative services. The last seven clinics in December will be as follows:

Dec. 15—Belleville, St. Elizabeth's Hospital.
Dec. 15—Effingham (rheumatic fever), St. Anthony Hospital.
Dec. 15—Peoria, Children's Hospital.
Dec. 16—Chicago Heights (general), St. James Hospital.
Dec. 17—Bloomington, St. Joseph's Hospital.
Dec. 17—Elmhurst, Memorial Hospital of DuPage County.
Dec. 17—Rockford, Rockford Memorial Hospital.

Chicago

Dr. Stollerman to Speak at Joint Meeting.—There will be a joint meeting of the Chicago Society of Internal Medicine and the Scientific Section of the Chicago Heart Association Dec. 14, 8 p. m., at the Drake Hotel. Dr. Gene H. Stollerman, associate professor of medicine, Northwestern University Medical School, will present "The Problem of Streptococcal Immunity in Rheumatic Fever Prevention." A dinner will precede the meeting which is open to all. For information, write Mr. Walter A. Rambach, Secretary, 720 N. Michigan Ave., Chicago 11 (Telephone: WH 4-0944).

Dr. Atkinson to Lecture at Ophthalmological Meeting.—Dr. Walter S. Atkinson, Watertown, N. Y., will present "Development of Ophthalmic Anesthesia" as the 16th annual Gifford Memorial Lecture at the 12th annual clinical conference of the Chicago Ophthalmological Society Feb. 12, 5:15 p. m., at the Drake Hotel. Subjects to be considered during the meeting Feb. 12-13 are as follows:

Symposium on Retinal Disorders.
Ophthalmodynamometry in Intracranial Vascular Disease.
Observations of Cataract Surgery.
Ultrasonography in Clinical Ophthalmology.
Photocoagulation of Iris and Retina.
A New Surgical Approach to Lacrimation Problems.
A Neurosurgeon Looks at Ophthalmology.
Ligament of Wieger.

The registration fee of $45 includes round-table luncheons and a dinner following the Gifford Lecture. For information, write Mrs. Mary E. Ryan, 1150 N. Lorel Ave., Chicago 51.

INDIANA

Program for Training in Family Practice.—A two-year educational program for young physicians aspiring to the role of family doctor and desiring

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

more clinical experience than a routine hospital internship has been developed by the Indiana University School of Medicine. The new family practice program follows suggestions of the American Medical Association and the American Academy of General Practice for such training but differs from similar programs now offered. The training period will consist of three divisions: The purpose of the first division is to familiarize the trainee with the functioning of those services in which he is later to work in a progressively more responsible capacity. It will consist of experience in the emergency room, medicine, pediatric, psychiatric, obstetrical, and gynecological services. The second division will encompass advanced experience in medicine and pediatrics. The third division will consist of elective work. The stipend is $2,400 for the first year and $2,700 for the second year. In addition, the trainee will enjoy all the privileges extended to the other members of the house staff. There are to be three appointments a year, and the selection is to be through the regular procedure of the Intern Matching Program. For information and applications, write to the Office of the Medical Director, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

KENTUCKY

Meeting of Surgeons in Louisville.—The American College of Surgeons will hold a sectional meeting Jan. 21-23 in Louisville. Headquarters will be the Brown Hotel. Dr. Rudolf J. Noer, of the University of Louisville School of Medicine, is chairman of the advisory committee on local arrangements. In addition to the general surgery program of particular interest to gynecologists, thoracic surgeons, vascular surgeons, and urologists, a special two-day ophthalmic surgery program, a special two-day program for otolaryngologists, and a cancer program workshop for medical directors of approved cancer programs are planned. Dr. Ernest C. Strode, Lexington, president of the Kentucky chapter of the college, will preside over the afternoon general surgery program, Jan. 21. Clinics will be held Jan. 23 at Louisville General Hospital. Medical motion pictures will be shown during the three days. Dr. H. Prather Saunders, associate director, The American College of Surgeons, 40 E. Erie St., Chicago 11, is in charge of all sectional meetings for the college.

MARYLAND

Rabies in a Bat.—Dr. Charlotte Silverman, Baltimore, of the Maryland State Department of Health, supplied a report from Dr. Charles L. Wisseman Jr., University of Maryland, Baltimore, of a suspected case of rabies in a bat, the first to be reported in Maryland. The bat was found fluttering erratically close to the ground in a residential area in Baltimore County. The bat was killed by a group of children and then abandoned. It was identified as the hoary bat, *Lasiurus cinereus*. Mouse-inoculation tests were performed and the first deaths occurred in the mice 21 days after the inoculation. Two additional mouse passages were done and the incubation period remained from 15 to 20 days. Smears prepared from the bat's brain revealed inclusion bodies suggestive, but not entirely typical, of Negri bodies. Fairly typical Negri bodies have been found in smears taken from the brains of the mice.

Hospital Plans to Move.—Sinai Hospital of Baltimore, Inc. plans to move from its present location at Monument Street and Rutland Avenue to its new quarters at Belvedere Avenue at Greenspring on Dec. 13, when some 150 to 200 patients will be transported to the new location. Located on a 50-acre site in northwest Baltimore, the new facilities of the hospital consist of 483 beds and 91 bassinets. Built at a cost of 20 million dollars, it includes a separate Research Building, Medical Staff Residence, School of Nursing, and Nurses' Residence. The expanded outpatient and emergency room facilities are designed to handle 100,000 outpatient visits a year. There are 19 ward beds with no more than two patients to a room, excepting in pediatrics. All patient areas are air-conditioned. The teaching and research program will remain in close association with Johns Hopkins University. A special scientific dedication is planned for Saturday and Sunday, April 23-24, 1960.

MICHIGAN

Lectures in Medical Psychology.—Dr. John I. Nurnberger, of Indiana University School of Medicine, Bloomington-Indianapolis, will deliver the Aquinas College Lectures in Medical Psychology for 1960 at the Aquinas College, Grand Rapids, on Wednesday, Feb. 24. Dr. Nurnberger, director of the Institute of Psychiatric Research at Indiana University, will speak once in the afternoon and again in the evening. A dinner in the college dining room will be served between the two lectures. In his first lecture Dr. Nurnberger will discuss sex and psychotherapy. His second lecture will be devoted to a discussion of the major manifestations of mental and emotional disorders as a guide to rapid diagnostic appraisal. Admission to the lectures will be limited to physicians.

Conference on Comparative Medicine.—The first annual Michigan Conference on Comparative Medicine will be held March 21-22, at the Kellogg Center for Continuing Education, Michigan State University, East Lansing. This conference will be sponsored jointly by the Michigan Department of Health, the University of Michigan Medical School, the Wayne State University College of Medicine, and the College of Veterinary Medicine at Michigan State University. Speakers on the program will include Dr. Jacob Furth, Roswell Park Memorial Institute, Buffalo; Dr. William L. Simpson, director, Detroit Institute of Cancer Research; B. R. Burmester, D.V.M., U. S. Regional Poultry Research Laboratory, East Lansing; W. E. Heston, Ph.D., head, General Biology Section, National Cancer Institute, Bethesda, Md., and Dr. Ludwik Gross, chief, Cancer Research Unit, Veterans Administration Hospital, Bronx, N. Y. Address inquiries to Mr. Clayton H. Wells, Conference Consultant, Kellogg Center for Continuing Education, Michigan State University, East Lansing, Mich.

MINNESOTA

Dr. Lundy Honored.—Some 75 former residents gathered at the Mayo Clinic in Rochester, Oct. 10, to honor Dr. John S. Lundy who retired after nearly 36 years of service as chairman of the section on anesthesiology. Dr. Lundy now is on the staff of the Veterans Research Hospital on East Huron Street, Chicago, and a consultant in anesthesia to several hospitals in Chicago.

NEW YORK

Dr. Caccamise Goes to India.—Dr. William C. Caccamise, Rochester, left Nov. 17 to conduct a free eye hospital for the medical missionary nuns of the Kurji Holy Family Hospital in Bihar, India. Dr. Caccamise will return Jan. 17. Some years ago he had conducted a free eye clinic in Bihar, which is 340 miles northwest of Calcutta on the banks of the Ganges River.

Radiation Center in Rochester.—The University of Rochester launched its new $400,000 radiation center at Strong Memorial Hospital, University Medical Center, Oct. 11 with a series of open houses for radiologists, professional people, and the personnel of the University of Rochester Medical Center. The radiation center is designed for diagnosis, therapy, teaching, and research in the problems of cancer and related diseases. Radiation machines include two supervoltage x-ray devices—a two-million electron volt Van de Graaff generating unit and a cobalt rotational unit. The center, housed in its own new building, also has two conventional orthovoltage 250 kilovolt range machines and a 140 kilovolt x-ray generator for treating surperficial lesions. Dr. Philip Rubin, chief of the division of radiation therapy, is director of the radiation center, and Dr. George H. S. Ramsey is chairman of the department of radiology, under which the division functions.

New York City

Vacancies for Radiology Training.—Opportunity for one year training in radiology (there are several vacancies available) with maintenance and honorarium, for anyone interested in learning radiology as an adjunct to his current specialty was announced by Dr. Henry K. Taylor, Roentgenologist, Goldwater Memorial Hospital, Welfare Island 17, N. Y. For information, write Dr. Taylor.

Dr. Rioch to Give Annual Lecture.—The Association for the Advancement of Psychoanalysis announced the eighth annual Karen Horney Lecture will be given by Dr. David McK. Rioch, director, division of neuropsychiatry, Walter Reed Army Institute of Research. The title is "Recent Contributions of Neuropsychiatric Research to the Theory and Practice of Psychotherapy." The meeting will be held on March 23, 8:30 p. m., at Hosack Hall, the New York Academy of Medicine, 2 E. 103rd St., New York City.

OHIO

Dr. Fischer Honored.—Dr. Martin H. Fischer, Cincinnati, was honored at ceremonies Nov. 10, on his 80th birthday. Highlight of the program was the presentation to the University of Cincinnati of an oil portrait of Dr. Fischer, which will hang in the College of Medicine building. Dr. Cecil Striker presented the portrait for the donors and his committee of Cincinnati doctors who studied with Dr. Fischer. Dr. Striker also presented a purse to the university to start a portrait fund for honoring other illustrious medical faculty members.

PENNSYLVANIA

State Medical Election.—Officers of the Pennsylvania Medical Society for 1959-1960 are: president, Dr. Allen W. Cowley, Harrisburg; president-elect, Dr. Thomas W. McCreary, Rochester; first vice-president, Dr. William T. Lampe, Philadelphia; second vice-president, Dr. Stephen J. Deichelmann, Ambler; third vice-president, Dr. John H. Lapsley, Indiana; fourth vice-president, Dr. Dorothy E. Johnson, Philadelphia; secretary, Dr. Harold B. Gardner, Harrisburg; and executive director and treasurer, Mr. Lester H. Perry, 230 State St., Harrisburg.

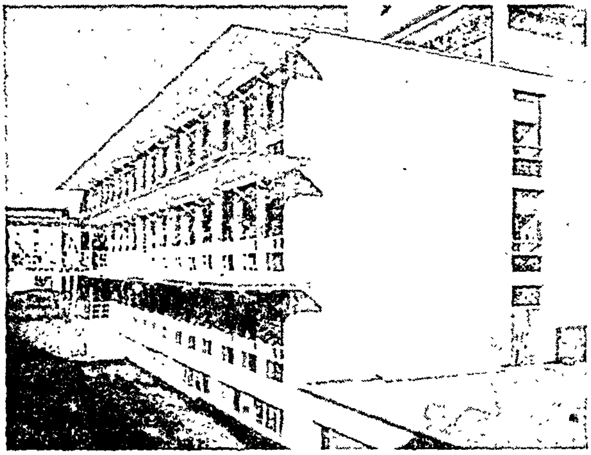
Philadelphia

Dr. Nemir Named Dean.—Dr. Paul Nemir Jr., associate professor of surgery in the University of Pennsylvania's Graduate School of Medicine, and assistant professor of surgical research in the School of Medicine, has been elected dean of the Graduate School of Medicine. He succeeds Dr. George B. Koelle, who resigned to accept the position of chairman of the departments of pharmacology in the School of Medicine and Graduate School of Medicine. Dr. Nemir was a fellow in the Harrison Department of Surgical Research at the University of Pennsylvania School of Medicine 1947-1951, later becoming an assistant professor in the department.

Hospital to Publish Semiannual Journal.—The medical staff of the Germantown Dispensary and Hospital will publish a semiannual scientific journal which will cover scientific material and research projects being carried out at the hospital. The first, to be ready by Jan. 1, will include articles on studies by the cancer research department (some of this work has been aided by the National Institutes of Health), results procured from new drugs which have been tested for pharmaceutical houses and reviewed as to their efficacy in medical practice, and a new approach to older laboratory procedures to reduce the margin of errors in certain situations. The journal will be available to county medical society libraries, as well as major research and diagnostic centers. Dr. Joseph C. Done is editor-in-chief and Dr. Irvin M. Gerson is managing editor.

RHODE ISLAND

Hospital Dedicates New Research Center.—The new George Research Center of the Rhode Island Hospital, Providence, was dedicated on Nov. 1. The three-story white brick and limestone structure for cancer diagnosis, treatment, and research was made possible by a bequest in the will of Daniel F. George, a Providence broker who died in 1949. The $2,100,000 building has no beds, but connecting corridors to the main building and other parts of the hospital facilitate transportation of patients to the cancer center. An auditorium seating 175 occupies part of the first floor. The remainder of this floor has multiple examining rooms and conference rooms. The second floor contains two cobalt treatment rooms, and rooms for superficial and deep x-ray therapy, plus diagnostic laboratories and autopsy rooms. The cancer library and registry are located on the third floor where research laboratories cover a large space. The entire building is air conditioned. Dr. Sidney Farber, professor of pathology, Harvard Medical School, and director of research of the Children's Cancer Research Foundation at Children's Medical Center, Boston, was the principal speaker at the dedicatory exercises.



The George Research Center of Rhode Island Hospital, Providence.

WISCONSIN

Fraternity Lecture.—The Alpha Psi Chapter of the Phi Delta Epsilon Fraternity at the University of Wisconsin Medical School, Madison, held its lectureship program on Friday, Dec. 11. The guest speaker was Dr. Solomon A. Berson, New York City, chief of the radioisotope service of the Bronx Veterans Administration Hospital. Dr. Berson spoke on the general topic of immunity aspects of insulin resistance and the nature of the insulin-antibody reaction.

WYOMING

Mental Health Clinic in Fremont County.—The first fully tax-supported mental health clinic in the state is being operated in Fremont County. The county is providing half the cost of operating the clinic with the remainder being paid by matching state funds. The city of Sheridan is the only other community to have a regular mental health clinic; however, it is supported by private subscription and matching state funds. Rev. William Watson is president of the Fremont County Mental Health Center, Inc. The clinic corporation is a nonprofit organization, formed to provide mental health services in Fremont County, and is governed by a nine-member board of directors. Clinics will be held in Lander from 8 a. m. to 5 p. m. in the offices of the public health nurse at the county courthouse. Professional staff includes three therapists from the State Training School at Lander. Supervision of the professional staff will be performed by Dr. Jesse E. Simons, State Health Department consulting psychiatrist. Patient fees will be collected to offset the cost of the service, "but no one will be turned away because of inability to pay." Clinic appointments will be limited to children.

GENERAL

Fund Aids Heart Research.—The Life Insurance Medical Research Fund aided 114 different heart research programs in the past year, according to the fund's annual report. In addition, 24 research fellows were supported. Nearly 1.2 million dollars were allocated for these research programs and fellowships, Dr. Francis R. Dieuaide, New York City, scientific director, said. Since 1945, when the fund was organized, its entire resources have been focused on heart disease. Thus far the fund has awarded a total of close to 12 million dollars for heart research programs and fellowships. Financial support comes from a membership of more than 140 life insurance companies in the United States and Canada.

Grant for Studies in Medical Communication.—The Institute for Advancement of Medical Communication, New York City, has received grant support from the U. S. Public Health Service for three current studies and projects aimed at improving intraprofessional communication in the medical sciences. A program for training investigators to study the general processes by which the results of medical research are disseminated, and by which the informational needs of research workers are met, is being supported by a grant from the National Heart Institute. The division of general medical sciences, National Institutes of Health has awarded a grant to organize the Council of Medical Television. The fate of information evolving from research in the new field of psychopharmacology is being studied under a grant from the National Institute of Mental Health.

Meeting of Ophthalmologists in New York City.—The Institute of Ophthalmology of the Americas will conduct a Post Pan-American Congress meeting at the New York Eye and Ear Infirmary Feb. 9-17. Each symposium will be composed of two Latin-American ophthalmologists and two infirmary staff members. The schedule is as follows:

Feb. 9, 10 a. m.—Cataracts.
Feb. 10, 10 a. m.—Retinal Detachment.
Feb. 11, 10 a. m.—Muscle Anomalies.
Feb. 12, 10 a. m.—Glaucoma.
Feb. 13, 10 a. m.—Uveitis.
Feb. 15, 10 a. m.—Keratectomies and Keratoplastics.
Feb. 16, 10 a. m.—Pleoptics and Macular Function Testing.
Feb. 17, 9 a. m.—Surgical Demonstrations on TV.

Invitations to attend may be obtained by writing to Mrs. Tamar Weber, Registrar, Institute of Ophthalmology of the Americas, New York Eye [illegible], 218 Second Ave., New York 3.

Seminar in Reconstructive Nasal Surgery.—A seminar in "Reconstructive Surgery of the Nasal Septum and External Nasal Pyramid" will be held in New Orleans, Feb. 10-13, under the auspices of the department of otolaryngology (Dr. Val Fuchs, chairman), Louisiana State University Medical School and the Charity Hospital. The American Rhinologic Society will cooperate in the presentation. Its founder, Dr. Maurice H. Cottle, professor of otolaryngology, Chicago Medical School, will be the guest director, and Dr. Henry A. Thomas, of L. S. U., will be the executive director. The seminar will offer talks by Dr. Cottle and others who have been invited to participate in an international course to be given in Mexico City, July 4-15, under the auspices of the Escuela Nacional de Medicina e Division del Doctorado, and the American Rhinologic Society. For information, write Dr. Robert M. Hansen, Secretary, American Rhinologic Society, 1735 N. Wheeler Ave., Portland 12, Ore.

Congress of Neurological Surgery.—The second International Congress of Neurological Surgery will be held at the Hotel Statler, Washington, D. C., Oct. 14-20, 1961. This conference is sponsored by the World Federation of Neurosurgical Societies, founded at Brussels in 1955. The first International Congress of Neurological Surgery was held in Brussels in 1957. The federation is presently composed of 25 national neurosurgical societies representing 50 nations. Four morning sessions will be devoted to symposiums on the following topics:

Radioactivity and Heavy Radiation Particles in Neurosurgery.
Space-Occupying Intracranial Lesions.
Reevaluation of Surgery in the Treatment of Pain.
A. Biology of the Nervous System; B. Hydrocephalus.

Voluntary papers are scheduled for presentation in the afternoons. A special feature will be daily television programs of operative procedures and panel discussions on neurosurgical techniques. Correspondence should be sent to Dr. Bronson S. Ray, Secretary-General, 525 E. 68th St., New York 21.

Fellowships in Radiology in Cincinnati.—The department of radiology of the University of Cincinnati College of Medicine and the Cincinnati General Hospital is offering three fellowships. One, in therapeutic radiology for radiologists who have completed their formal residency training, is for one year with a stipend of $6,000. Another fellowship, in radiobiology, radioisotopes, and radiological research techniques, is offered to physicians who have completed their formal residency training and is not restricted to radiologists. The appointment is for one year with a stipend of $6,000. A third fellowship with a stipend of $2,000 is open to physicians who have completed internship or some part of their residency training and is designed to acquaint the fellow with research techniques utilizing radioisotopes and other radiation sources. The latter two fellowships are currently available and new openings will occur on July 1, 1960. Interested physicians should communicate with the Department of Radiology, University of Cincinnati College of Medicine, General Hospital, Cincinnati 29.

Society News.—Mr. William Kloepfer Jr. was appointed director of public information for the **Pharmaceutical Manufacturers Association,** with headquarters in Washington, D. C., effective Nov. 13.——Dr. Isidore S. Ravdin, Philadelphia, was named president-elect of the **American College of Surgeons** at the annual meeting of fellows Oct. 2, succeeding Dr. Owen H. Wangensteen, Minneapolis, who became president. Dr. Charles C. Higgins, Cleveland, was chosen first vice-president-elect; Dr. Allen M. Boyden, Portland, second vice-president-elect; and Dr. William E. Adams, Chicago, was elected secretary of the college.—— The officers of the **American College of Preventive Medicine** are: president, Dr. James H. Sterner, Rochester, N. Y.; president-elect, Dr. John D. Porterfield III, Washington, D. C.; vice-president for public health, Dr. Roy L. Cleere, Denver; vice-president for aviation medicine, Dr. Theodore C. Bedwell Jr., Omaha; vice-president for occupational medicine, Dr. Melvin N. Newquist, New York City; and secretary-treasurer, Dr. John J. Wright, P. O. Box 1267, Chapel Hill, N. C.——The **Central Society for Clinical Research** elected the following officers for the society for 1960: president, Dr. John H. Dingle, Cleveland; vice-president, Dr. Gordon Meiklejohn, Denver; and secretary-treasurer, Dr. Austin S. Weisberger, Cleveland.

FOREIGN

Congress of Endocrinology in Copenhagen.—The first International Congress of Endocrinology will be held in Copenhagen from July 18-23, 1960. The program will consist of 10 symposiums and a round-table discussion and of groups of shorter (10-minute) communicated papers. Speakers at the symposiums and the round-table discussion are investigators in the field of endocrinology, and titles and abstracts are invited. Forms for registration in the congress, along with forms for the submission of abstracts of short communications, may be obtained by writing to the Congress Secretariat, Dr. Svend G. Johnsen, Hormone Department, Statens Seruminstitut, Copenhagen S, Denmark. The final date for the submission of such abstracts is Dec. 31. The languages of the congress are English, French, German, and Spanish. Titles and abstracts of communicated papers should not be sent to the Program Committee, but the committee will review and arrange for the presentation of such papers in appropriate congress sessions.

CORRECTION

Treatment of Tuberculosis.—In the abstract entitled "Observations on the Treatment of Pulmonary Tuberculosis with Sulfoniazid" in The Journal, Oct. 31, page 1267, the dose should have been 0.5 Gm., not 50 Gm.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II, Various Cities, April 19-20. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 21-23. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Delaware: *Examination.* Dover, Jan. 12-14. *Endorsement.* Dover, Jan. 21. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Examination.* Honolulu, Jan. 11-12. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination* and *Reciprocity.* Boise, Jan. 11, 12, 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Indiana: *Examination.* Indianapolis, June 1960. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Kansas:* *Examination and Reciprocity.* Kansas City, Jan. 15-16. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Massachusetts: *Examination.* Boston, Jan. 12-15. Sec., Dr. David W. Wallwork, Room 37, State House, Boston.

Minnesota:* *Examination.* Jackson, June 1960. *Reciprocity.* Jackson, Dec. 7, Sec., Dr. A. L. Gray, Old Capitol, Jackson.

Nebraska:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

New Jersey: *Examination.* Jan. 19-22. *Reciprocity.* Monthly, Admin. Sec., Michael E. H. Sweeney, 28 West State St., Trenton.

North Dakota: *Examination.* Grand Forks, Jan. 6-8. *Reciprocity.* Grand Forks, Jan. 9. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

Oregon:* *Examination.* Portland, Jan. 12-13. *Reciprocity.* Portland, Jan. 14-16. Ex. Sec., Mr. Howard J. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination.* Philadelphia, January. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

Utah: *Examination.* Salt Lake City, July 6-8. *Reciprocity.* Salt Lake City, Nov. 17. Director, Mr. Frank E. Lees, 324 State Office Bldg., Salt Lake City 1.

Washington:* *Examination.* Seattle, Jan. 11-13. Administrator, Professional Division, Capitol Bldg., Olympia.

West Virginia: *Examination.* Charleston, Jan. 11-13. Sec., Dr. Newman H. Dyer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:* *Examination.* Madison, Jan. 14-16. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Building, 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, Feb. 1. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Washington: *Examination.* Seattle, Jan. 6-7. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

AIR FORCE

School of Aviation Medicine.—The research and educational facilities of the Aerospace Medical Center at Brooks Air Force Base, San Antonio, Texas, were opened to the press and invited dignitaries Nov. 12 to 14. Dedication ceremonies for the center's new school of aviation medicine on Nov. 14 were preceded by a private press tour of the laboratories which are searching for the secrets of sustaining human life during space flights. Sen. Lyndon B. Johnson addressed the assembled military and scientific leaders.

General Byrnes Awarded Legion of Merit.—Brig. Gen. Victor A. Byrnes, who retired on Sept. 30, was presented prior to his retirement with the Legion of Merit by Major Gen. Oliver K. Niess, the surgeon general. He received the award for his outstanding professional ability and his vision and leadership in his role as director of professional services in the office of the surgeon general.

ARMY

Medical Officers to Train in India.—The Calcutta School of Tropical Medicine and Hygiene in India will be a training ground for Army preventive medicine specialists in an agreement recently concluded by the U. S. Army Medical Service and the school. Through this arrangement, Dr. R. N. Chaudhuri, dean of the school, will accept an Army physician as a resident observer on his staff for three months with spaces rotating among Army internists, preventive medicine officers, and occasionally other clinical specialists. Thus each year four officers may participate in this program. They will study such major communicable diseases as plague, cholera, dysentery, and smallpox—diseases which are rarely seen in the United States.

At present, medical officers receive similar training through tropical medicine fellowships offered by the Louisiana State University. In this program, four officers study tropical diseases in Central America each year. Major Jerome H. Greenberg, M. C., a preventive medicine officer in the Army surgeon general's office, will be the first participant in the program at the Calcutta School of Tropical Medicine and Hygiene. He will be there from early November, 1959, to February, 1960.

Medically Important Mosquitoes.—Richard R. Foote and David R. Cook of the Department of Agriculture have prepared a handbook entitled "Mosquitoes of Medical Importance," which should enable military and civilian entomologists to identify mosquitoes in any part of the world. It will serve as an invaluable aid in the prevention and control of mosquito-borne diseases that now are a scourge of many tropical countries. The Army medical service requested and supported this project because of a lack of suitable guides for entomologists during World War II, when mosquito-borne diseases were a major military problem, particularly in the Pacific areas. A unique feature of the book is a series of more than 60 pictorial keys, which will be of aid to persons having a minimum of training in identifying mosquitoes. Published as Agriculture Handbook no. 152, this book may be obtained without charge from the Entomology Research Division, Agricultural Research Service, U. S. Department of Agriculture, Washington 25, D. C.

Personal.—Dr. Myles Maxfield, formerly with the medical department of the Brookhaven National Laboratories, Upton, N. Y., was appointed chief of the physical science division at Fort Detrick, Md.——Col. Adam J. Rapalski, M. C., was appointed commanding officer, U. S. Army Environmental Health Laboratory at the Army Chemical Center, Md. He replaces Col. Edward J. Dehne, M. C., who has been assigned as preventive medicine officer, headquarters, Second U. S. Army, Ft. Meade, Md.

NAVY

Three-Hundred-Foot Rise from Submarine.—On Oct. 1 two men surfaced from a depth of 300 ft. They were Commander George F. Bond, M. C., U. S. N., officer in charge of the Naval Medical Research Laboratory, and chief engineman C. G. Tuckfield, instructor at the New London Submarine Escape Training Tank. This event demonstrated that it is feasible for submarines to escape from great depths with the new "blow and go" method of submarine escape. The unique feature of this method is that the escapee does not wear any type of breathing appliance. He wears a life jacket, which carries him to the surface. The sequence of events in making the escape are as follows: The men who are to escape enter the submarine escape lock and close the doors. Water is admitted into this lock from the sea until the pressure within the escape lock is the same as the sea pressure. At 302 ft. this pressure would be about 135 lbs. per square inch. This has the effect of filling the escapee's lungs with highly compressed air. The escapee then inflates his life jacket with air, opens the door to the escape lock, and steps out. He then ascends to the surface—the buoyancy being provided by the life jacket—exhaling continuously as the reduced pressure expands the air in his lungs. During the escape 25 seconds were required to pressurize the escape lock. The ascent required 53 seconds.

New Training Program.—The Naval Medical Research Unit no. 2 at Taipei, Formosa, has organized a training program to provide opportunities for scientists in foreign countries to use the equipment at their laboratory to carry on research in virology, parasitology, clinical investigation, and entomology. Provisions have been made for at least 12 research fellows from several countries in the Far East to study under the program.

Personal.—Rear Adm. Cecil L. Andrews was appointed assistant chief of the bureau of medicine and surgery for personnel and professional operations.——Capt. Merrill H. Goodwin was named assistant chief of the bureau of medicine and surgery for Aviation Medicine and director of the Aviation Medicine Operations Division after the retirement of Capt. Oran W. Chenault in September.——Capt. C. F. Gell, M. C., special assistant for medical and allied sciences, was elected chairman of the subcommittee on acceleration and bioassay techniques for human centrifuges at the recent meetings of the aeromedical panel of NATO's advisory group for aeronautical research and development. The subcommittee will study problems of international standardization of nomenclature and bioassay end-points for centrifuges.——Capt. Oran W. Chenault, assistant chief of the bureau of medicine and surgery for aviation medicine for the past two years, retired in September after 29 years of service.

PUBLIC HEALTH SERVICE

Cancer Control Program.—The Public Health Service has created a 14-member advisory committee to its Cancer Control Program. The committee will help state and local agencies to develop services to decrease the interval between the discovery of new cancer techniques and their application. One of the duties of the new committee will be to pass on applications for $1,500,000 in federal grants for community cancer demonstration projects.

The Cancer Control Program, under the direction of Dr. Lewis C. Robbins, is in the division of special health services, Bureau of State Services. The members of the advisory committee are (1) Dr. Ulrich R. Bryner of Salt Lake City; (2) Dr. Bernard Bucove, director, Washington State Department of Health; (3) Dr. John W. Cline, associate clinical professor of surgery at Leland Stanford University; (4) Dr. Warren H. Cole, professor of surgery at the University of Illinois College of Medicine; (5) Dr. Joseph A. Cunningham, professor of pathology at the University of Alabama; (6) Dr. Harold S. Diehl, deputy executive vice-president of the American Cancer Society; (7) Dr. Lloyd M. Graves, associate professor of preventive medicine at the University of Tennessee College of Medicine; (8) Dr. John P. Lindsay, Nashville, Tenn.; (9) Dr. James J. Nickson, professor of radiology at Cornell University Medical College; (10) Dr. Mack I. Shanholtz, Commissioner of Health for the State of Virginia; (11) Dr. Charles E. Smith, professor of public health at the University of California; (12) Dr. John W. Spellman, clinical professor of surgery at the Medical School of Tufts College; (13) Dr. Samuel G. Taylor III, clinical associate professor of medicine at the University of Illinois College of Medicine; and (14) Dr. David A. Wood, professor of pathology at the University of California School of Medicine.

Health Characteristics of Children.—The extent to which acute illnesses and injuries are concentrated among children is documented in a report by the Public Health Service's National Health Survey.

The report discloses that in the year ending June 30, 1958, young children suffered acute illnesses with twice the frequency of adults. The incidence rates for acute illnesses involving either restricted activity or medical attention ranged from a high of 4.0 occurrences a year for children under 5 years of age to a low of 2.0 occurrences for adults 25 and over. On the other hand, adults over 25 averaged almost twice as many days of restricted activity from illness or injury as persons under 25. For different age groups under 25, the days of restricted activity per person per year ranged from 13.2 to 16.4, as compared with 24.1 days for adults over 25.

Home accidents among children under 15 years of age were the chief cause of injuries restricting activity or requiring medical attention. They were an important cause, along with motor vehicle and work accidents, of restricted activity in the 15-to-24-year age group. The report also gives figures, for persons under 25, on impairments and limitation of activity and mobility due to chronic conditions, hospital discharges, physician visits, and dental visits. The estimates were derived from interviews conducted by the U. S. Bureau of the Census with a representative sample of the civilian, noninstitutional population. The new report is entitled "Children and Youth, Selected Health Characteristics, United States, July 1957–June 1958," Public Health Service publication no. 584-C 1. Copies may be obtained from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 35 cents each.

Personal.—Dr. Sam Silbergeld was appointed to a staff position in the research grants branch of the division of general medical sciences, National Institutes of Health. Dr. Silbergeld transferred from the National Institutes of Health division of biologics standards, where he was staff assistant to the director.

DEATHS

Anderson, Joseph Gordon, Lake City, Fla.; Southern College of Medicine and Surgery, Atlanta, 1914; served with the U. S. Public Health Service; veteran of World War I; died in the Veterans Administration Hospital Aug. 11, aged 67.

Aronson, Emma Selkin Ⓜ New York City; Woman's Medical College of Pennsylvania, Philadelphia, 1910; fellow of the American College of Surgeons; associated with the staff of the Bronx Hospital, which presented her with a special bronze plaque "for many years of distinguished service"; member of the staff of the New York Infirmary and in 1956 recipient of its Elizabeth Blackwell Citation, for "outstanding contribution to the knowledge of medicine"; died Sept. 24, aged 72.

Arscott, William W., Rogers City, Mich.; Saginaw (Mich.) Valley Medical College, 1903; veteran of World War I; director of the Rogers City Band; honorary member on the medical staff of the Rogers City Hospital, where he died Sept. 7, aged 88.

Bare, Samuel Luther Ⓜ Westminster, Md.; University of Maryland School of Medicine, Baltimore, 1905; member of the American Academy of General Practice; vice-president of the Carroll County National Bank; associated with the Maryland General Hospital, Baltimore, where he died Sept. 26, aged 76.

Barnes, Benjamin Franklin Ⓜ Chattahoochee, Fla.; Marion-Sims College of Medicine, St. Louis, 1901; served as secretary and treasurer of the Jefferson County Medical Society; died in the Frasier-Ellis Hospital in Dothan, Ala., Sept. 11, aged 82.

Barney, Benjamin Arthur Ⓜ Hornell, N. Y.; Long Island College Hospital, Brooklyn, 1897; past-president of the Medical Society of the State of New York and the Steuben County Medical Society; served on the staffs of St. James Mercy and Bethesda hospitals; a director and past-president of the Maple City Cooperative Savings and Loan Association; died in the Williamsport (Md.) Sanitarium Sept. 19, aged 87.

Bates, Charles Oscar Ⓜ Greenville, S. C.; born in Spartanburg in 1886; University of Georgia Medical Department, Augusta, 1909; member of the Southeastern Surgical Congress and the Industrial Medical Association; fellow of the American International College of Surgeons and the American College of Surgeons; a member and past-president of the Southern Railway Surgeons Association; a member of the Greenville City Board of Health for many years and was serving as chairman; associated with the Greenville and St. Francis hospitals; member of the board of directors of the Peoples National Bank; died in the Greenville General Hospital Sept. 15, aged 73.

Borden, Frederic Wallace Ⓜ San Jose, Calif.; born in Spokane, Wash., Dec. 9, 1893; Stanford University School of Medicine, San Francisco, 1929; served as secretary and president of the Santa Clara County Medical Society, as president of the Visiting Nurses' Association, and on the board of directors of the local American Red Cross; from 1942 to 1947 chairman of the Procurement and Assignment Committee; invented the Borden Hemorrometer, for continuous measurement of blood loss during surgery; instrumental in the commercial development of the Stanford X-Ray Stereoscope; on the staffs of the O'Connor and San Jose hospitals; died in the Children's Hospital in San Francisco Sept. 24, aged 65.

Boswell, Brown Hill Ⓜ Robertsdale, Ala.; Tulane University School of Medicine, New Orleans, 1945; interned at the James M. Jackson Memorial Hospital in Miami, Fla., and the Touro Infirmary in New Orleans; formerly a resident at the Orange Memorial Hospital in Orlando, Fla.; died in South Baldwin Hospital, Foley, Sept. 15, aged 41.

Calder, James Ralph Ⓜ Long Beach, Calif.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1947; interned at Royal Victoria Hospital in Montreal, Que., and Ste. Anne's Hospital in Ste. Anne de Bellevue, Que.; served an internship and residency at the Queen Mary Veterans Hospital in Montreal, Que.; associated with the St. Mary's Hospital where he died Aug. 18, aged 39.

Callander, Russell John Ⓜ Solana Beach, Calif.; Rush Medical College, Chicago, 1919; member of the American College of Chest Physicians; fellow of the American College of Physicians; veteran of World War II; for many years associated with the Veterans Administration Hospital in Mountain Home, Tenn.; died Sept. 12, aged 67.

Carpenter, Grant Stephen, North Sacramento, Calif.; Minneapolis College of Physicians and Surgeons, *medical* department of Hamline University,

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Ⓜ Indicates Member of the American Medical Association.

1901; formerly assistant superintendent of the North Dakota State Hospital for Insane, Jamestown; died Sept. 15, aged 89.

Cohen, Morris, Brooklyn; Fordham University School of Medicine, New York City, 1916; first deputy medical superintendent of Kings County Hospital, where he died Sept. 25, aged 67.

Cook, Albert Edward, Caldwell, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1903; died in Montclair Aug. 29, aged 81.

Craft, William Fletcher, Linton, Ind.; Indiana University School of Medicine, Indianapolis, 1915; veteran of World War I; served as health officer of Green County and of Linton; died Sept. 8, aged 73.

Curry, Claud Allen Ⓜ Terre Haute, Ind.; Indiana University School of Medicine, Indianapolis, 1920; past-president of the Vigo County Medical Society; Union Hospital staff treasurer for many years; died Sept. 20, aged 65.

Dech, Elmer Jesse Ⓜ Easton, Pa.; Eclectic Medical Institute, Cincinnati, 1894; at one time practiced in Pandora, Ohio, and served as coroner of Putnam County; died in the Easton Hospital Sept. 15, aged 88.

Dick, Edward Joseph Ⓜ Syracuse, N. Y.; Syracuse University College of Medicine, 1909; on the staff of the Crouse-Irving Hospital; died Sept. 18, aged 72.

Dion, George J., New Bedford, Mass.; Middlesex College of Medicine and Surgery, Waltham, 1930; also a pharmacist; died in St. Luke's Hospital Sept. 11, aged 68.

Dorger, Philip Henry, Covington, Ky.; Medical College of Ohio, Cincinnati, 1909; veteran of World War I; for many years on the staff of the St. Elizabeth Hospital; died Sept. 18, aged 74.

Everett, Eugene Ellsworth Ⓜ Port Charlotte, Fla.; Harvard Medical School, Boston, 1899; died in the Lee Memorial Hospital, Fort Myers, Aug. 27, aged 98.

Fischer, Edward Frederick Ⓜ Alton, Ill.; Barnes Medical College, St. Louis, 1910; on the staffs of St. Joseph's Hospital and the Alton Memorial Hospital, where he died Sept. 22, aged 77.

Flinn, James Edgar, Pittsburgh; Cleveland Homeopathic Medical College, 1904; veteran of World War I; on the staff of the Shadyside Hospital; died Sept. 16, aged 79.

Formusa, Anthony Carl Ⓜ Melrose Park, Ill.; University of Illinois College of Medicine, Chicago, 1915; died in St. Mary Mercy Hospital, Gary, Ind., Sept. 29, aged 66.

Gardner, Carol Elissa Ⓜ Montgomery, Ala.; Columbia University College of Physicians and Surgeons, New York City, 1942; interned at the Charity Hospital in New Orleans and the Harper Hospital in Detroit; served a residency at the Herman Kiefer Hospital in Detroit; for many years chief radiologist for the Veterans Administration regional office of Alabama; died Sept. 15, aged 41.

Geib, Henry Albert Ⓜ Milford, Conn.; University and Bellevue Hospital Medical College, New York City, 1914; at one time associated with the New York State Board of Health; died in Hartford Sept. 12, aged 75.

Gramling, James Walter, Gadsden, Ala.; Medical College of Alabama, Mobile, 1901; associated with the Baptist Memorial Hospital; died Sept. 6, aged 81.

Grubb, Andrew Bayne, Cripple Creek, Va.; University College of Medicine, Richmond, 1909; died Sept. 21, aged 73.

Haskell, Henry Alfonso Ⓜ Philadelphia; Howard University College of Medicine, Washington, D. C., 1929; died Sept. 28, aged 57.

Haynes, Frederick Eugene, Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1899; veteran of World War I; for many years associated with the city health department; died Sept. 16, aged 83.

Horton, Ralph Ⓜ Oneonta, N. Y.; born in Jane, Mo., Jan. 13, 1901; University of Kansas School of Medicine, Kansas City, Kan., 1926; specialist certified by the American Board of Preventive Medicine; past-president of the Otsego County Society; fellow of the American College of Chest Physicians and the American College of Physicians; member of the American Trudeau Society and the American Public Health Association; in 1946 appointed general director of the tuberculosis hospitals of the New York State Department of Health and in 1932 to its division of tuberculosis; at one time associated with the U. S. Public Health Service; associate in medicine at the Albany (N. Y.) Medical College; medical director of the Homer Folks Tuberculosis Hospital; consultant, Aurelia Osborn Fox Memorial Hospital; in 1931-1932, member of the medical staff, Loomis Sanatorium in Liberty; died Sept. 17, aged 58.

Josewich, Alexander Ⓢ Minneapolis; University of Minnesota Medical School, Minneapolis, 1914; member of the American Trudeau Society; for many years associated with the Veterans Administration; formerly chief of the tuberculosis service, Veterans Administration Hospital; veteran of World War I; died Sept. 19, aged 69.

Karr, John Welch Ⓢ Jamestown, N. Y.; born in Keene, Ohio, Sept. 6, 1906; University of Rochester School of Medicine and Dentistry, 1936; specialist certified by the American Board of Radiology; member of the American Society of Clinical Pathologists and the Radiological Society of North America; served on the faculty of his alma mater and the University of Utah College of Medicine in Salt Lake City; member of the Atomic Energy Commission from 1948 to 1950; formerly associated with the Rochester (N. Y.) General Hospital, Strong Memorial and Monroe County hospitals in Rochester, N. Y.; in 1950-1951 associated with the Salt Lake City General Hospital and the Veterans Administration Hospital in Salt Lake City; on the staffs of the Westfield (N. Y.) Memorial Hospital, Woman's Christian Association Hospital, and Jamestown General Hospital; died Sept. 17, aged 53.

Keil, George William, Columbus, Ohio; Columbia University College of Physicians and Surgeons, New York City, 1912; for many years chief medical officer at the Ohio Penitentiary Hospital; died Sept. 21, aged 72.

Kenyon, John Marcus Ⓢ Richland, Ga.; University of Nashville (Tenn.) Medical Department, 1893; Vanderbilt University School of Medicine, Nashville, Tenn., 1893; died Sept. 17, aged 89.

Kornreich, Eugene Frederick Ⓢ Chagrin Falls, Ohio; Western Reserve University School of Medicine, Cleveland, 1924; died in the Veterans Administration Hospital, Cleveland, Sept. 21, aged 64.

Kruger, Rudolph Arthur Samuel Ⓢ Brockton, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1926; member of the American Academy of General Practice; from 1928 to 1932 served as city physician; died Sept. 18, aged 57.

Landes, Herbert Ellis Ⓢ Chicago; Rush Medical College, Chicago, 1922; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; professor and chairman of the department of urology, Stritch School of Medicine of Loyola University; on the staffs of the City of Chicago Municipal Tuberculosis Sanitarium and the Mercy Hospital; died Sept. 24, aged 64.

Larkin, Ernest Waddill, Washington, N. C.; North Carolina Medical College, Charlotte, 1917; veteran of World War I; died in the Beaufort County Hospital Sept. 21, aged 70.

Lindsay, Guion Alton Ⓢ Dallas, Texas; Memphis (Tenn.) Hospital Medical College, 1902; associated with St. Paul Hospital, where he died Sept. 15, aged 79.

Losa, Lada Paul Ⓢ Homestead, Pa.; University of Pittsburgh School of Medicine, 1923; served in France during World War I; on the staff of the Homestead Hospital, where he died Sept. 14, aged 63.

McCoy, Mary Knauf Ⓢ Duluth, Minn.; University of Michigan Medical School, Ann Arbor, 1890; served on the faculty of her alma mater; died Sept. 14, aged 99.

McLeod, James Harvey, Santa Rosa, Calif.; Marion-Sims College of Medicine, St. Louis, 1896; past-president of the Sonoma County Medical Society; died Sept. 15, aged 90.

McQueeney, Andrew Michael Ⓢ Bridgeport, Conn.; born in New Haven, June 22, 1882; Yale University School of Medicine, New Haven, 1905; fellow of the International College of Surgeons and the American College of Surgeons; past-president of the Bridgeport Medical and Fairfield County Medical societies; served as member and president of the board of education; formerly member of the board of directors of the department of welfare and of the board of governors of the City Dispensary; for many years chief of the surgical staff of St. Vincent's Hospital; died Sept. 20, aged 77.

Mayer, Emil Valentine Ⓢ Highland Park, Mich.; Loyola University School of Medicine, Chicago, 1916; veteran of World War I; on the staffs of the Highland Park (Mich.) General Hospital and the Mount Carmel Mercy Hospital, where he died Sept. 16, aged 73.

Messmer, Anthony Conrad Ⓢ Ardmore, Pa.; Jefferson Medical College of Philadelphia, 1920; served as house physician for the Rosemont (Pa.) College and the Villanova (Pa.) College; associated with the Thomas M. Fitzgerald Mercy Hospital in Darby and the Bryn Mawr (Pa.) Hospital, where he died Sept. 25, aged 70.

Miller, Eugene Leo Ⓢ Newark, N. J.; Long Island College of Medicine, Brooklyn, 1937; vice-president of the New Jersey Dermatological Society; served as a flight surgeon during World War II, holding the rank of major; awarded the Air Medal in 1944 and the Distinguished Flying Cross in 1945; on the staffs of St. James and Presbyterian hospitals, and the Martland Medical Center; died in the Memorial Hospital, New York City, Sept. 19, aged 46.

Morton, James Alexander Ⓜ Pontiac, Mich.; University of Michigan Medical School, Ann Arbor, 1942; interned at the State of Wisconsin General Hospital in Madison, Wis., where he served a residency; specialist certified by the American Board of Radiology; member of the American College of Radiology; chief of radiology department, St. Joseph's Mercy Hospital; captain in the U. S. Army Reserve from May 1953 to May 1955; died Sept. 16, aged 42.

Murphy, John Patrick, St. Louis; Washington University School of Medicine, St. Louis, 1912; died June 9, aged 70.

Needham, Frank Stewart Ⓜ Oak Park, Ill.; Dearborn Medical College, Chicago, 1905; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908; from 1918 to 1938 health commissioner of Oak Park; for many years served on the council of the American Medical Milk Commissioners and as chairman of the ethical relations committee of the Chicago Medical Society, of which he was past-president of the Aux Plaines Branch; served as president of the Oak Park and River Forest Physicians' Club; associated with the West Suburban Hospital and the Oak Park Hospital, where he died Sept. 22, aged 82.

Neuland, William Ⓜ New York City; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1914; died aboard the SS New Amsterdam while on a trip to Europe June 29, aged 68.

Neumann, Gottfried Ⓜ New York City; Universität Leipzig Medizinische Fakultät, Saxony, Germany, 1933; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons and the American Academy of Obstetrics and Gynecology; assistant clinical professor of obstetrics and gynecology, New York University College of Medicine; veteran of World War II; on the staff of the University Hospital, where he was chief of the sterility clinic, New York University-Bellevue Medical Center; on the staff of the Beth Israel Hospital, where he died Sept. 26, aged 58.

Newman, Henry Wise Ⓜ San Francisco, Stanford University School of Medicine, San Francisco, 1931; specialist certified by the American Board of Psychiatry and Neurology; member of the Harvey Cushing Society, American Neurological Association, and the American Academy of Neurology; professor of medicine at his alma mater; veteran of World War II; served on the staffs of the U. S. Naval Hospital in Oakland, Calif., and the Veterans Administration Hospital; died in Belvedere, Calif., Sept. 19, aged 52.

O'Connell, Edward Ⓜ Birmingham, Ala.; University and Bellevue Hospital Medical College, New York City, 1907; fellow of the American College of Surgeons; past-president of the Birmingham Surgical Society; for many years on the Jefferson County Board of Health; served on the staff of St. Vincent's Hospital; died Sept. 16, aged 75.

Pearson, Robert Garfield Jr., Sacramento, Calif.; University of California School of Medicine, San Francisco, 1954; interned at the University of California Hospital in San Francisco; died Sept. 18, aged 34.

Perri, Angelo Marco Ⓜ Philadelphia; Jefferson Medical College of Philadelphia, 1925; associate professor of public health and preventive medicine at the Hahnemann Medical College and Hospital of Philadelphia; for many years chief of the division of communicable diseases of the city department of health and since 1956 director of the medical center; a director of the Crime Prevention Association; member of the American Public Health Association; died at his summer home in Plymouth Meeting Sept. 18, aged 58.

Raine, Maxwell Francis, Crane, Texas; Ohio State University College of Medicine, Columbus, 1929; formerly health officer of Kanawha County, W. Va.; at one time health officer in Mason, Jackson, Putnam, and Roane counties, W. Va.; on the staff of the Crane County Memorial Hospital; died Sept. 11, aged 55.

Ransom, Matthias Lent Ⓜ Hancock, Minn.; Jefferson Medical College of Philadelphia, 1902; died in the Stevens County Memorial Hospital, Morris, Aug. 27, aged 85.

Reese, Emmett Francis Jr. Ⓜ Courtland, Va.; University College of Medicine, Richmond, 1899; member and past-chief of staff, Raiford Memorial Hospital in Franklin; member of the board of directors of the Southampton County Bank; died Sept. 26, aged 82.

Ring, Dean Merrill Ⓜ Major, U. S. Air Force, retired, Cedar Rapids, Iowa; State University of Iowa College of Medicine, Iowa City, 1951; interned at the University of Minnesota Hospitals in Minneapolis, where he served a residency; served a residency at the Veterans Administration Hospital in Nashville, Tenn.; specialist certified by the American Board of Surgery; chief of surgery at the Ladd Air Force Base in Alaska from 1956 to 1958 when he became chief of surgery at Chanute Air Force Base, Ill., where he died in the U. S. Air Force Hospital Sept. 17, aged 32.

Rizzolo, Edward Michael Ⓜ Belleville, N. J.; Baylor University College of Medicine, Dallas, 1925; during overseas duty in World War I, received the Croix de Guerre, French medal for bravery; associated with the Presbyterian, St. Michael's, and American Legion Tri-County Memorial hospitals in Newark; died in the East Orange (N. J.) General Hospital Sept. 21, aged 61.

Rosa, Henry Antonio Ⓜ Portsmouth, R. I.; Baltimore Medical College, 1899; served as medical examiner of the Portsmouth District; while practicing in Fall River, Mass., served on the board of health, and as chairman of the board of trustees of the Fall River General Hospital; died in the Truesdale Hospital in Fall River, Mass., Sept. 19, aged 84.

Roth, Aaron, Brooklyn; University and Bellevue Hospital Medical College, New York City, 1908; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; veteran of World Wars I and II; on the staff of the Beth El Hospital; formerly on the staffs of the Gouverneur Hospital in New York City, Brooklyn Women's Hospital, and the Brooklyn Jewish Hospital, where he died Sept. 9, aged 72.

Rowley, Howard Frederick Ⓜ Rochester, N. Y.; University of Michigan Medical School, Ann Arbor, 1920; specialist certified by the American Board of Pediatrics; past-president of the Rochester Pediatric Society; member of the American Academy of Pediatrics; on the staffs of the Strong Memorial and Rochester General hospitals; died Sept. 23, aged 64.

Schurter, Raymond Joseph, St. Louis; St. Louis University School of Medicine, 1923; since 1957 chief of communicable disease control for the St. Louis City Department of Health; served on the staffs of St. Mary's Hospital in East St. Louis, and St. Anthony's Hospital and St. Mary's Infirmary; died Sept. 23, aged 62.

Seabolt, Gertrude Clowes, Pasadena, Calif.; University of Southern California College of Medicine, Los Angeles, 1907; for many years school physician; died Sept. 15, aged 78.

Shaw, Alexandre, Flushing, N. Y.; University of Tomsk Faculty of Medicine, Siberia, Russia, 1923; died in the Kew Gardens (N. Y.) General Hospital Sept. 20, aged 63.

Sneed, John William, Nashville, Tenn.; University of Nashville Medical Department, 1901; died Sept. 16, aged 82.

Steinbach, Simon, St. Petersburg Beach, Fla.; Universitatea din Bucuresti Facultatea de Medicina, Rumania, 1901; for many years practiced in New York City; died Sept. 16, aged 84.

Talley, Oran Hubbell Ⓜ Corpus Christi, Texas; University of Texas School of Medicine, Galveston, 1911; veteran of World War I; since 1939 physician for American Smelting and Refining Company; died Sept. 11, aged 74.

Tessier, Claude Edward, Augusta, Ga.; Medical College of Georgia, Augusta, 1932; interned and served a residency at the Wilhenford Hospital for Women and Children and the University Hospital, where he was a member of the staff, and where he died Sept. 12, aged 54.

Van Dyke, Joseph Smith Ⓜ Palisades Park, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1903; for 25 years school physician; for many years on the staff of the Englewood (N. J.) Hospital, where he died Sept. 9, aged 84.

Van Tine, Edward Postlethwaite Ⓜ Wynnewood, Pa.; Hahnemann Medical College and Hospital, Philadelphia, 1928; specialist certified by the American Board of Anesthesiology; member of the American Society of Anesthesiologists, Inc.; assistant professor of anesthesiology at his alma mater; chief of anesthesiology at Delaware County Hospital in Drexel Hill; died Sept. 12, aged 56.

Vetter, James Harry Ⓜ Rockford, Ill.; Rush Medical College, Chicago, 1916; served in France during World War I; member of the honorary staff, Rockford Memorial Hospital; died in the Rockford Municipal Tuberculosis Sanitarium, Sept. 3, aged 69.

Wagner, Robert Lowell Ⓜ Captain, U. S. Navy, La Jolla, Calif.; born in San Bernardino Jan. 6, 1908; McGill University Faculty of Medicine, Montreal, Que., Canada, 1935; interned at the San Francisco Hospital in San Francisco; served a residency at the Lane and Stanford University hospitals in San Francisco; formerly a fellow in psychiatry at Neuro-Psychiatric Institute of the Hartford Retreat in Hartford, Conn.; veteran of World War II; specialist certified by the American Board of Psychiatry and Neurology; head of the neuropsychiatric service at the U. S. Naval Hospital in San Diego, where he died Sept. 7, aged 51.

Weigen, Anders John Ⓜ Chicago; Rush Medical College, Chicago, 1914; member of the American Academy of Pediatrics; trustee of the Chicago Medical Society and past-president of the North Shore Branch; veteran of World War I; member of the staffs of the Children's Memorial Hospital, Augustana Hospital, and the Swedish Covenant Hospital, where he died Sept. 27, aged 70.

Weiser, Frank Andrew, Detroit; Detroit College of Medicine and Surgery, 1920; served on the faculty of Wayne University College of Medicine; formerly editor-in-chief of the *Detroit Medical News;* associated with the Receiving Hospital of the City of Detroit and the Wayne County General Hospital and Infirmary, Eloise; on the staff of the Grace Hospital, where he died Sept. 9, aged 64.

Wilcox, James Whedon Ⓜ Bay City, Mich.; Detroit College of Medicine and Surgery, 1932; member of the American Academy of General Practice; past-president of the Bay County Medical Society; chairman of the airport advisory committee of the James Clements Airport; on the staffs of the General and Mercy hospitals; died in Ranger Lake, Ont., Canada, Sept. 5, aged 52.

Wilkins, Josiah S., Hot Springs National Park, Ark.; Memphis (Tenn.) Hospital Medical College, 1913; on the staffs of the Leo N. Levi Memorial Hospital, Quachita General Hospital, and St. Joseph's Hospital, where he died Sept. 15, aged 81.

Williams, Albert Evan, Fountain City, Wis.; Milwaukee Medical College, 1908; veteran of World War I; on the staffs of St. Joseph's Hospital in Arcadia and City Hospital, Menomonie; died Sept. 10, aged 78.

Williams, Russel Hill Ⓜ Fort Lauderdale, Fla.; Ohio State University College of Medicine, Columbus, 1925; for many years head of the student health service, Denison University in Granville, Ohio; died Sept. 14, aged 67.

Williams, Warren Henry Ⓜ Manlius, N. Y.; born in Utica, N. Y., Sept. 24, 1922; Cornell University Medical College, New York City, 1948; certified by the National Board of Medical Examiners; specialist certified by the American Board of Radiology; interned at the Milwaukee County Hospital in Milwaukee and the Syracuse Memorial Hospital in Syracuse; served a residency at the Syracuse University Medical Center in Syracuse, N. Y., and the University of Texas M. D. Anderson Hospital and Tumor Institute in Houston; on the faculty of the State University of New York Upstate Medical Center in Syracuse; captain in the Army Medical Corps from 1952 to 1954; on the staff of the Crouse-Irving Hospital in Syracuse, where he died Sept. 15, aged 36.

Wilson, Richard H. Ⓜ Martins Ferry, Ohio; Barnes Medical College, St. Louis, 1898; fellow of the International College of Surgeons and the American College of Surgeons; a director of the Fidelity Savings and Loan Company; served as vice-president and director of the Peoples Savings Bank; associated with the City Hospital in Bellaire and the Barnesville (Ohio) Hospital; founder and chief surgeon of the Martins Ferry Hospital, where he died Sept. 11, aged 85.

Woods, Thomson Butler, South Norfolk, Va.; University of Maryland School of Medicine, Baltimore, 1913; veteran of World War I; died in Norfolk Sept. 4, aged 70.

Zinkhan, Paul Hudson, Ravenna, Ohio; Georgetown University School of Medicine, Washington, D. C., 1912; veteran of World War I; for many years served on the board of education; in 1949 honored by the Ravenna Junior Chamber of Commerce, which presented him its outstanding citizen's award for his work on behalf of the community; past-president of the Portage County Medical Society; on the staff of the Robinson Memorial Hospital; died Sept. 4, aged 74.

Zilboorg, Gregory Ⓜ New York City; born in Kiev, Russia, Dec. 25, 1890; University of Helsingfors, Russia, 1917; Columbia University College of Physicians and Surgeons, New York City, 1926; served in the medical corps of the Russian Army; participated in the first revolution in Petrograd in 1917 when he was secretary to the Ministry of Labor in Cabinets of Lvov and Kerensky; forced to leave Russia and came to the United States in 1919; clinical professor of psychiatry at the State University of New York College of Medicine at New York City, Brooklyn, and New York Medical College, Flower and Fifth Avenue Hospitals; visiting professor of psychiatry at Fordham University; on the faculty of Woodstock (Md.) College, and the mental health institute at St. John's University in Collegeville, Minn.; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychoanalytic Association and the Association for Research in Nervous and Mental Diseases; in 1953 received the Isaac Ray Award of the American Psychiatric Association, of which he was a member and an academic lecturer; president of the scientific commission of the International Criminology Society; secretary and director of research, Committee for the Study of Suicide; chairman of the Consulting Delegation on Criminology to United Nations; vice-president of the third International Congress on Criminology in London; last February was the second speaker in a lecture series sponsored by the Boston University Law-Medicine Research Institute; associate visiting psychiatrist, Kings County Hospital and consulting psychiatrist at St. Vincent's Hospital; author of four books in his field; died in the Lenox Hill Hospital Sept. 17, aged 68.

FOREIGN LETTERS

GERMANY

Metabolism After Total Pancreatectomy.—E. Kühnlein (*München. med. Wchnschr.* 101:1592, 1959) stated that the few cases of long survival after total pancreatectomy in human beings have demonstrated that it was possible to substitute for, and balance, the secretory losses after the loss of the gland. The amount of insulin required after total pancreatectomy was strikingly low and ranged in long-surviving patients from 30 to 40 units a day. Only in those with complications, febrile affections, or insulin resistance due to development of antibodies against insulin were larger doses required. The lasting sensitivity of these patients to insulin was pronounced. This was mainly due to the great loss of glucagon-producing cells.

As far as the exocrine function of the pancreas was concerned, difficulties were mainly encountered with regard to fat metabolism and to a lesser degree to that of proteins. Individual patients varied widely as to the severity of their digestive insufficiency. Further difficulties (osteoporosis) may be incurred by increased loss of calcium and manifestations of vitamin deficiency. The danger of fatty changes in the liver, however, is relatively small. Only one case of diabetic retinopathy after total pancreatectomy has been reported. Whether the frequency of vascular damages corresponds to that of spontaneous diabetes cannot yet be decided. Derivatives of sulfonylurea are ineffective in diabetic patients after pancreatectomy, but biguanids seem effective. A patient who has undergone a total pancreatectomy requires continuous careful medical supervision, but in general his life is endurable and worth living.

Cardiac Surgery.—Successful operation for ventricular aneurysm or diverticulum in three children was reported by Derra and Loogen of Düsseldorf (*Deutsche med. Wchnschr.* 84:1585, 1959). A 9-year-old boy was operated on in 1952. The left ventricular aneurysm was not resected, but the myocardial defect was closed with a pursestring suture placed in the superficial myocardial layers, and the aneurysmal wall was sutured over it. In the other two patients (an 8-year-old boy and 17-year-old boy) the aneurysm was resected and the myocardial defect closed with multilayered sutures during circulatory arrest under hypothermia. In the older boy the aneurysm of the right ventricle had developed after a previous transventricular pulmonary valvotomy for pulmonary stenosis. The pulmonary valve was opened during one period of circulatory arrest and the aneurysm was resected during a second. Radiologic examinations postoperatively, including angiocardiography, showed some myocardial bulging in the first patient but normal ventricular movements in the other two. The previously high operative mortality should be markedly reduced as a result of the introduction of hypothermia and the heart-lung machine. Resection or extirpation of the aneurysm or diverticulum with well-placed, multilayered sutures through the myocardium is considered the method of choice. In certain patients plastic ventricular repair may be indicated.

Hereditary Cortisone Deficiency.—H. G. Fassbender of Mainz (*Deutsche med. Wchnschr.* 84:1595, 1959) observed two brothers who had cortisone deficiency. One died at 7 years of age and an autopsy showed the classic picture of precocious pseudopuberty as part of the adrenogenital syndrome with hypertension due to bilateral adrenal cortical hyperplasia. Their father, who died at 47 years of age and was also examined post mortem, had severe hypertensive renal and vascular lesions, a hypopotassemic myocardium, renal tubular changes, and—like his sons—cutaneous hyperpigmentation. It was assumed that father and sons had a similar, gene-determined cortisone deficiency. In the two boys the disordered steroid formation led predominantly to the production of androgens and less so of mineralocorticoids, while in the father the reverse condition existed.

INDIA

Preeclampsia.—Menon and Ramanamma (*J. Indian M. A.*, vol. 33, Sept. 16, 1959) used Veratenshun (a combination of protoveratrine with reserpine and other alkaloids of Rauwolfia) to treat 140 patients with preeclampsia. The preparation for intravenous injection contained 0.15 mg. of protoveratrine, 2.5 mg. of reserpine, and 4 mg. of Rauwolfia alkaloids per milliliter and each tablet contained 0.2 mg. of protoveratrine, 0.15 mg. of reserpine, 3 mg. of Rauwolfia alkaloids, 15 mg. of phenobarbitol, 15 mg. of pentaerythritol tetranitrate, and 2 mg. of homatropine methyl bromide. In this series 90 patients were in the antenatal period and of these 20 had a mild toxemia with blood pressure readings of 140 to 160 mm. Hg systolic and 90 to 100 mm. Hg diastolic, slight albuminuria and edema, and mild or absent symptoms; 50 patients were in labor and in all of these the toxemia was severe.

The items in these letters are contributed by regular correspondents in the various foreign countries.

All patients were treated on admission by bed rest, sedatives, a salt-poor diet, and acetazolamide. After 48 hours Veratenshun was given in addition to the other measures being used. The patients with mild symptoms received one tablet two or three times a day, increasing by one tablet daily till the optimum dose (not more than eight tablets per day) was reached. Most of these patients were 34 to 36 weeks pregnant. Of the severe cases, 12 patients were given the tablets but responded poorly. They were therefore given 1 ml. of the preparation intravenously in 20 cc. of 20% dextrose solution and their blood pressure was recorded at short intervals. Orally given therapy was then used as supplement. If no hypotensive effect occurred after the first injection, it was repeated at intervals of 6 to 8 hours till a maximum of three in 24 hours was reached. The duration of treatment varied. In 75% of the patients it ranged from 4 to 15 days; one patient received it for 70 days.

Labor was induced prematurely only if the response was poor and the patient's condition deteriorated. In the mild cases, oral therapy produced no significant benefit, the results being the same even without the use of the hypotensive drug. In severe cases, oral therapy alone was of no use but helped in maintaining hypotensive or normotensive levels after the blood pressure was brought down by intravenous injections. In 80%, the level came down in 15 minutes after injection. The maximum drop was 110 mm. Hg systolic and 70 mm. Hg diastolic. The higher the systolic pressure initially, the greater was the drop after injection. The hypotensive effect lasted 1 to 26 hours. Although the response was poor in only 11.4% of those who used the drug as compared to 40% in the controls, the drug did not help in reducing the prematurity or the perinatal death rate. No untoward effects on mother or fetus were attributable to the Veratenshun. It was thus found useful in controlling blood pressure rise in labor.

Liver in Malnutrition.—Sheth and Warerkar (*Indian J. Child Health,* vol. 8, September, 1959) studied 27 patients with protein malnutrition. The liver was palpable below the costal margin in 21 and edema was present in 19. The thymol turbidity, alkaline phosphatase level, and cephalin-cholesterol flocculation were determined in 25 patients. The first was altered in three patients and the second in six; the flocculation test result was positive in six. There was no correlation between the findings of the three tests. The degree of abnormality in liver function and the degree of edema did not correspond. Similarly there was no correlation between the degree of liver enlargement and liver function.

The plasma protein levels of 26 patients were estimated; 18 patients showed reversal of albumin-globulin ratio. The patient with the highest protein value (7.3 Gm.) showed such a reversal and had edema. The severity of the edema and the degree of protein deficiency did not show any correlation as patients without edema also had low protein values, with reversal of the albumin:globulin ratio. Paper electrophoresis was done in five cases and showed a fall of albumin in all, which was the least in the patients without edema. In three patients, alpha-1 and alpha-2 globulin levels were increased, one had a fall in alpha-1 and alpha-2 and another had reduction in alpha-1 and an increase in alpha-2. The beta globulin level was lowered in all and the gamma globulin level was reduced in three, normal in one, and raised in another. The fibrinogen level was raised in all. A liver biopsy was performed on 15 patients with no failure and no untoward effects. The prominent lesion was fatty infiltration. Although connective tissue was seen in some specimens, none showed cirrhotic changes.

Tuberculin Reactors.—A. K. Basu and co-workers (*Indian J. Child Health,* vol. 8, September, 1959) studied 500 children attending a pediatric clinic and selected at random to determine whether any correlation existed between tuberculin sensitivity and such factors as poverty, overcrowding, ventilation of dwelling, state of nutrition, and previous attacks of acute illness. The reading after tuberculin injection was taken on the third day and chest roentgenograms were taken of all positive reactors. Of the 500 children, 133 or 26.6% showed a positive reaction. The percentage of reactors increased with age. Thus, up to one year of age only 12.7% were positive reactors but 80% of the age group 7 to 12 fell in this category. The percentage of positive reactors varied inversely with the economic status of the family. More than half of the positive reactors lived in rooms of average ventilation but the same was true of nonreactors. Of the children living in one-or-two-room dwellings, 33 to 50% were positive reactors, but of those living in three to five-room homes only 25% were positive reactors. Most of the children in both groups came from families with four to seven members. Nourishment did not appear to have much influence on the tuberculin reaction.

More than half the reactors gave a history of acute illness (measles in 54.8%, whooping cough in 18.8%, repeated colds in 81.2%, and chronically infected tonsils in 56.4%). Of the positive reactors 10% had demonstrable primary tuberculous lesions in the lungs and 40% of the reactors had no radiological evidence of tuberculosis. Thirteen reactors gave a history of contact with tuberculous patients and 13 nonreactors also gave such a history. Only 8.3% of the positive reactors had a demonstrable primary lesion in the lung while 76 had a healed primary focus in the lung and 46 had a clear roentgenogram of the chest. In these either the primary focus had healed completely or it was located elsewhere in the body.

Toxemias of Pregnancy.—S. Subrahmanyam (*Indian J. M. Sc.*, vol. 13, September, 1959) stated that increased urinary excretion of adrenocortical metabolites occurring in toxemias of pregnancy suggests an increased activity of the adrenal cortex resulting in fluid and electrolyte imbalance and such symptoms as edema, hypertension, increase in body weight, and proteinuria. Whether the adrenal medulla also plays some part in this condition was studied by the author by investigating 25 normal women, 25 normal pregnant women, 100 women with preeclampsia, and 7 with eclampsia. The patients with toxemias had blood pressures higher than 140 mm. Hg systolic and 90 mm. Hg diastolic, edema, and albuminuria.

After collecting a 24-hour sample of urine, half of it was used to determine the 17-ketosteroid content and the other half to estimate the catechol amines. The levarterenol excretion rates were 33.8, 36.3, and 68.3 mcg. in normal women, normal pregnant women, and women with toxemias respectively. The corresponding figures for epinephrine excretion were 5.7, 6.5, and 9.4 mg. The average excretion of levarterenol, epinephrine, and 17-ketosteroids was higher in those with toxemias than in normal women and normal pregnant women. The epinephrine excretion was more than in normal women but its percentage was lower than in the other two groups. The 17-ketosteroid excretion was slightly increased in normal pregnancy but in patients with toxemia it was almost double that found in normal women. The same was true of levarterenol excretion. Thus the activity of both the adrenal cortex and the medulla was increased in patients with toxemia. The excess of circulating levarterenol and epinephrine in these patients may have been responsible for their hypertension.

Genital Tuberculosis.—S. Bose (*J. Obst. & Gynec.*, India, vol. 10, September, 1959) reported a series of 80 women with genital tuberculosis. This involvement was tubal in 43, endometrial in 26, and cervical in 11. Cervical lesions were commonest in the age group 21 to 30 years. Of those with tubal involvement 15 had tuberculous peritonitis. Only six had pulmonary lesions associated with endometrial tuberculosis. There was no instance of urinary or skeletal involvement in the series. The lesions were mostly miliary with isolated tubercles and peritoneal nodules. Sixteen had matted tubo-ovarian masses with dense adhesions. Pyosalpinx containing caseous material and few adhesions was found in only one patient. The endometrium presented a normal appearance on gross examination in most patients. Ulcerative and proliferative cervical lesions were equally distributed and four were erroneously diagnosed carcinoma. In nine sterility was the primary complaint and others were found to have been infertile for several years. Menorrhagia or metrorrhagia was present in 34 and amenorrhea in 13. Ten had abdominal pain and 13 had distention associated with involvement of the pelvic peritoneum. Only four had low-grade fever and debility.

The usual treatment initially consisted of 1 Gm. of streptomycin and 10 Gm. of PAS daily for three months; 150 to 200 mg. of isoniazid was given daily if no appreciable improvement occurred or toxic manifestations appeared. An operation was performed only when the diagnosis was in doubt (8) or the patient did not respond to medical treatment (25). Twenty had panhysterectomy; in 9 there were extensive miliary tubercles on the peritoneum, omentum, and intestines and the abdomen was closed after peritoneal instillation of streptomycin; 2 had salpingectomy; and 2 had an amputation of the cervix. Intensive antituberculous treatment was continued during the postoperative period. There were no deaths.

SWEDEN

Child Accident Rate Reduced.—Intensified propaganda in Sweden for the safety of children has greatly reduced the number of fatal accidents among them, according to Dr. Ragnar Berfenstam who addressed the ninth International Congress of Pediatrics in Montreal, Canada. One result of the safety campaign was that the number of drownings among children in the ages between 10 and 14 years had dropped by about 50% over the past 40 years. The number of children per unit of population killed or injured by poison in Sweden is one of the lowest in the world. The safety campaign was largely organized by the country's pediatric clinics. Safety catches for windows, safe ovens, child-proof caps for bottles containing medicines or dangerous chemicals, and safe electrical outlets have been introduced. Moreover, the manufacturers of baby articles have given valuable advice on packaging. In the domestic science classes at school the girls are taught how to protect children against accidents.

Doctors Recommend Health Identity Card.—The steadily rising number of Swedes who travel by car at home and abroad and the large increase in serious traffic accidents has brought about appreciable medical problems. An international identity and health card containing basic medical data would help in solving these problems, according to Drs. Ored Arner and Matts Halldin of Stockholm. Most accidents necessitate a quick and adequate shock treatment of the injured, blood transfusion, and treatment against tetanus. A health and identity card would here be of immense value, as it would also aid in the treatment of acute cases of illness occurring abroad. The card should contain name and address of the owner and next-of-kin, language spoken and understood, blood group, medical data such as earlier immunizing injections, treatment with hormones, and information about hypersensitiveness and whether the owner suffers from diabetes or epilepsy. To be of value abroad the card should be written in Swedish, English, French, German, Spanish, and Finnish.

Acromegaly.—Dr. C. A. Hamberger and co-workers (*Nordisk medicin*, Sept. 3, 1959) removed the pituitary gland by the transantrosphenoidal route in 10 patients with acromegaly. Good results could be claimed in seven patients with regression of the external manifestations of the disease. In the four patients in whom complete insufficiency of the gland was demonstrable, these external changes were most noticeable. These patients were given substitution treatment with cortisone and thyroid extract, supplemented in one with testosterone. Normal thyroid and adrenal functions were retained in the other patients. The severe headache from which two patients had suffered ceased, menstruation returned, and pregnancy went to term in one patient. No signs of activation were observed in follow-up periods of two months to three years. The authors stressed the fact that radiologic treatment with the dosage hitherto given has seldom or never achieved any essential regression of the disease.

Future of Mental Welfare.—In 1955 the Swedish Medical Association and the Swedish Psychiatric Society urged the government to explore the means by which mental welfare of the country could be adequately provided. The opinions of various scientific bodies were presented in *Svenska läkartidningen* (Sept. 25). Its authors confessed to a certain bewilderment over having to draw up housing plans in the distant future for psychiatric patients at a time when psychiatric practices are changing so fast. To what extent, they asked, will modern treatment be more effective in a closed institution than in the patient's home? They answered this question by remarking that it has become more and more desirable to treat the patient while he is engaged in normal work and lives in home surroundings. The organization of health work in industry has also promoted extramural, rather than intramural, care of the mental patient. A grave risk is often run when a patient is taken from a normal environment to the regimented atmosphere of a hospital. There must always be a residue of incurable, chronic mental patients who require hospital treatment, but even among those with senile psychosis some are amenable to modern treatment. Psychiatric hospital planning comes thus to be largely guesswork, and it is suggested that the mental hospital of the future should be planned on the basis of five beds per thousand of the population.

Generalized Herpes Zoster.—Although the sequence of herpes zoster followed by a generalized eruption of the varicella type is so rare that only about 100 such cases have been reported, Floderus and Rolander (*Nordisk medicin*, Sept. 24, 1959) observed six such cases in 113 days in a hospital in Luleå (population about 29,000). In five of these patients the interval between the onset of the zoster lesion and that of the general eruption was one, four, six, six, and eight days respectively. A raised gamma globulin fraction in two of these patients suggested that the ability to form antibodies had been retained by them. This syndrome occurred in one man with previously unrecognized lymphatic leukemia. Other observers have noted a similar connection between the two ailments. The authors concluded that herpes zoster, varicella, and generalized herpes zoster are caused by the same virus, and that the accumulation of six cases in a short period must have been due to a change in the virulence of this virus.

Prochlorperazine in Psychiatry.—In the past two years about 100 psychiatric patients were treated at the St. Jörgen Hospital with prochlorperazine. In addition to slight and moderately severe cases of degression and "mental insufficiency," chiefly in women, there were 14 patients who had chronic schizophrenia, and in some of these Dr. B. Wetterholm and co-workers (*Svenska läkartidningen*, Sept. 11, 1959) had surprisingly good results. In some of these patients the dosage was 75 mg. daily, and in others good results were obtained with 15 to 30 mg. a day. The drug proved useful as a supplement to electroshock when it had failed to achieve a satisfactory remission. In other patients the drug was effective as a supplement to chlorpromazine. It was also helpful in patients undergoing treatment for addiction to barbiturates. Even with small doses the drug might cause paralysis agitans, and it might render the patient drowsy, but it caused no serious side-effects, and no addiction to it was observed. In two nurses contact dermatitis developed, but the liability to sensitivity reactions, so troublesome for the hospital staff in the case of chlorpromazine, was much less marked.

Porphyria.—Dr. J. Waldenström (*Nordisk medicin*, Oct. 1, 1959) reported that of the two most common forms of porphyria, the acute intermittent form and porphyria cutanea tarda, the former is represented by some 500 known cases in Sweden. Apparently examples of both forms never occur in a single family, each porphyria family presenting its typical biochemical and clinical features. Repeated studies with sensitive biochemical tests showed that apparently healthy carriers can now be positively identified. At one time manifest porphyria was credited with a case fatality rate of 50 to 60%, but this could be much reduced by a correct and early diagnosis and by the avoidance of barbiturates and general anesthesia. If, instead of giving the patient much fluid and intestinal irrigation to promote peristalsis, he is rushed to the hospital with the mistaken diagnosis of intestinal obstruction and operated on under sedatives and general anesthesia, severe paralyses may set in, terminating in death. Porphyria cutanea tarda, with late development of hypersensitivity to light, is also probably an inherited disorder whose symptoms can be evoked by the ingestion of much alcohol. Both forms of porphyria would seem to depend on a genetically determined enzyme defect which manifests itself definitely under the influence of specific toxins.

UNITED KINGDOM

Coe Virus.—During laboratory investigations connected with a trial of adenovirus vaccine at Royal Air Force recruiting stations, four strains of an agent with a cytopathic action on HeLa-cell cultures were isolated. This agent had some properties of enteroviruses but could not be identified with any known members of this group. It proved to be identical with an agent named Coe virus isolated from Army recruits in California. Pereira and Pereira investigated its prevalence in Britain by means of a serologic survey (*Lancet* 2:539, 1959). Throat swabs were taken from patients with respiratory illness. The virus was isolated from those who, in addition, had cervical adenitis, hoarseness, conjunctivitis, and chest and muscle pains. The virus was identified by its cytopathic effects on HeLa-cell cultures and propagation in cultures of human amnion and a cell line of embryonic rabbit kidney. The presence of antibodies in serums of persons in different age groups was investigated by serum neutralization tests.

The survey revealed a low rate of infection with Coe virus in children. The incidence gradually rose with age. Thus, at ages 61 to 70 years, 71% of the men and 52% of the women showed antibodies to the virus. The mean incidence in males, taking all age groups into consideration, was twice that of females. This might have been due to the greater chances of males to become infected in the armed forces and in industry due to close personal contact.

Trivalent Poliomyelitis Vaccine.—Relatively little has been reported on the simultaneous administration by mouth of the three types of poliomyelitis vaccine or on the oral use of mixtures of them as a trivalent vaccine. This is because certain strains of poliovirus tend to interfere with the establishment and multiplication of other strains in the intestines. It has now been found possible to maintain a mixed infection of types 2 and 3 poliovirus for at least 20 serial passages in monkey kidney tissue culture. Dr. H. R. Cox and co-workers reported the results of giving orally a liquid poliomyelitis vaccine, containing attenuated types 1, 2, and 3, to 550 adult volunteers (*Brit. M. J.* 2:591, 1959). All persons involved were under close medical surveillance.

Serologic studies were made on 241 of the volunteers. Only 3 of the 550 persons reported any illness in the two months after the vaccine was given. The serum was titrated for antibodies three months after oral vaccination. The number of persons responding to the trivalent vaccine was higher for types 3 and 1. The best results, judged by primary conversions or a titer increase of at least fourfold, were obtained in those persons receiving the larger dose of vaccine, namely 1,200,000 tissue culture 50%-infectious doses (TCD_{50}) of each of the three types of poliovirus in 2 ml. of vaccine. Although good, the antibody responses to 300,000 and 600,000 TCD_{50} were lower. The conversion rate of 188 persons receiving the largest dose was 93%. These results indicated that it is both possible and practicable to immunize against all three types of poliovirus by giving a single dose of a trivalent poliovirus vaccine by mouth. These highly favorable results were obtained in adults. It is believed that children are even more readily immunized with poliovirus vaccine given by mouth.

Medical Members of Parliament.—Twenty-one physicians ran for Parliament at the general election in October, 8 on the Conservative, 11 on the Labor, and 2 on the Liberal ticket. Of these 10 were returned as members of Parliament (5 as Conservative and 5 as Labor members). Both of those who ran as Liberals failed to be elected.

Skin Grafting in Twins.—The blood of newborn nonidentical cattle twins usually contains erythrocytes of two distinct serologic types. This is attributed to the exchange of blood in intrauterine life since cattle twins are commonly synchorial. The condition, known as blood chimerism, is practically unknown in man, only two cases of such twins having been reported. This is of interest because it is a manifestation of immunological tolerance of hemologous tissue. Skin homografts exchanged between nonidentical cattle twins may survive for long periods, or even permanently, without regard to differences of sex or color, in contrast to homografts between human nonidentical twins or siblings which are rapidly destroyed.

Woodruff and Lennox (*Lancet* 2:476, 1959) made a skin grafting experiment on a pair of human blood chimeras of different sex, the second pair to be reported in the literature. They were 21 years old and each contained erythrocytes of groups A and O in the ratio of 86:14 in the male twin and 1:99 in the female twin. The twins generously consented to submit to reciprocal skin grafting. A full thickness skin graft 1 cm. square was removed from the volar aspect of the wrist of each twin under local anesthesia, and the grafts were interchanged at the site of removal.

The grafts took well and have now persisted in each twin for two years. The graft on the male twin behaved macroscopically like an autograft. That on the female twin was deeper in color than her normal skin and retained the coarser pattern of surface markings characteristic of male skin. The graft on the male twin was microscopically normal skin which was unmistakably male on nuclear sexing. That on the female twin was also microscopically normal. In nuclear sexing the tissue at the end of the biopsy specimen was female, while that in the center was male. Blood grouping showed that the twins at this time were still blood chimeras.

The findings suggested that the female twin was completely tolerant of her brother's skin. Nuclear sexing showed that in the male this was not so, nearly all the cells of the grafts having been replaced by cells of host origin. This, however, does not imply that the graft was immunologically unacceptable, as even autologous bone grafts may be replaced. This experiment is of interest because hitherto it has not been possible to induce tolerance to homologous tissue in man.

Acrylic Resins for Intracranial Aneurysms.—The treatment of intracranial aneurysms by investing them with acrylic resin was described by Dutton, who followed up 17 patients treated in this way (*Brit. M. J.* 2:597, 1959). Initially acrylic resin implants and vessel investments were made in the brains of goats to study the immediate and delayed vascular and cellular effects. Although a mild microglial and astrocytic reaction was produced in the molecular layer of the cortex, there was no evidence of damage to the nerve cells or to the vessels. Difficulty arose in sterilization as acrylic resin cannot be boiled or autoclaved. It was therefore sterilized by exposure to 2 to 3 million rads from the cobalt bomb. This did not affect the polymerization of the powdered polymer resin. The monomer, which when mixed with the polymer solidifies, was sterilized by Seitz filtration. The polymer and monomer were mixed in empty dental anesthetic cartridges, and after standing until the right consistency was reached the cartridge was put in a syringe and the viscous resin extruded through a cannula. The resin was allowed to flow around the cerebral vessel and sac, forming a collar which was molded to the required shape.

Only those aneurysms were so treated that were technically difficult to ligate or clip. Hence in three years only 17 patients with subarachnoid hemorrhage due to aneurysms were found to be suitable for acrylic investment. Nine of these had aneurysms of the anterior communicating artery and eight had aneurysms of the middle cerebral artery. The latter group did uniformly well, with no deaths. There were four deaths in the former group. At autopsy the aneurysmal sacs were satisfactorily invested by the acrylic resin, and no bleeding had occurred at the site of the aneurysm.

Breast Feeding.—In his annual report for 1958, Prof. A. B. Semple, health officer for Liverpool, described a survey on breast feeding conducted for a period of eight months, during which 7,272 mothers with babies six weeks of age were questioned. The proportion of breast-fed infants was the same (about 25%) regardless of whether the confinement took place in the hospital or in the home. Of 3,963 mothers with normal breast development and an adequate milk supply 52% asked the doctor or the clinic to suppress lactation. Of these 25% obtained tablets for this purpose from the hospital and 70% obtained the tablets from their general practitioners. About 4% obtained such tablets from pharmacists.

Breast abscesses accounted for about 6% of cases in which lactation was suppressed. In spite of the known danger of the spread of infection in hospitals, the incidence of sepsis in infants born in hospitals was about the same as that in infants born at home—10.6% and 10.1% respectively. Breast abscess and sepsis in the infant showed a close correlation. Some evidence of sepsis was present in 23.4% of the babies of mothers who had been delivered in the hospital. The sepsis figure for babies born at home was 71.7%. The incidence of sepsis was nearly 10% in the babies of mothers with normal breasts who had been delivered in the hospital and just over 9% in the babies of mothers delivered at home.

Society for Social Medicine.—At the third annual meeting of the Society for Social Medicine held in Dundee Prof. Alex Mair described the hazards of jute manufacture, which is the major industry of the town. It has long been known in Dundee that workers in the jute industry suffer from chronic respiratory disease, but no specific pneumoconiosis syndrome, such as that occurring in cotton workers, has ever been described. Careful examination revealed that flax workers suffer from a byssinosis-like condition due to inhaled dust.

Dr. L. R. Lowe gave some interesting facts on absenteeism and works injuries in relation to smoking habits. The incidence of works injuries declines with age but increases with the amount of tobacco smoked, provided the influence of the association of age with smoking habits is eliminated by standardization. The mean number of days absent for illness increased both with age and with the amount smoked. A relation was established between the amount smoked and the incidence of works injuries, and this was more apparent in the younger workers. The association of smoking with absence for medical reasons was more apparent in the older group. Dr. Lowe attributed the latter to respiratory illness caused by, or exacerbated by, smoking in older persons.

Dr. R. Acheson and Prof. W. Jessop described the results of a study of the serum proteins in men who had spent their lives working in a large brewery. Gamma-globulin levels increased with age after 65 years. Albumin levels were significantly higher in those who ate meat twice a day than in those who ate it less often. Men who drank more than 12 pints of beer a day showed an increased beta globulin level.

Treatment of Warts by Hypnosis.—For many centuries warts have been charmed away by fortune tellers and the like. The treatment of warts by hypnotic suggestion is described in the medical literature, but its value is difficult to determine owing to the lack of controlled trials and the possibility of spontaneous recovery. Sinclair-Gieben and Chalmers (*Lancet* 2:480, 1959) described a controlled trial on the treatment of warts by hypnosis. In a pilot study the warts of six patients disappeared within three months when treated by medium deep hypnosis; 14 patients were then treated by well-established methods of inducing hypnosis, such as relaxation, darkness, eye fixation, and repetitive commands. Once a state of hypnosis was induced it was suggested that the warts on one side of the body would disappear and that on awakening the patient would perform some specified action as described. Only patients with bilateral and multiple common warts of at least six months' duration were admitted to the trial, and only one side of the body was treated. This was always the side with the larger warts. Ten patients reached an adequate depth of hypnosis and four did not.

The time taken for cure on the treated side was between five weeks and three months. In the four patients whose hypnosis was only slight no benefit was obtained. If the original 6 patients are included 16 of 20 consecutive patients could be hypnotized to an adequate depth. The matched controls showed that the cure of warts can be effected by hypnosis. Improvement was always on the treated side, but the hypnosis must reach a certain depth. Those who lost their warts all showed posthypnotic suggestion in that after awakening they had performed actions suggested to them. In those who got no benefit such suggestion had failed.

Aspergillin O.—Stefanini and co-workers, who previously reported that a strain of Aspergillus oryzae (B-1273) produced a substance with a highly selective fibrinolytic activity, have obtained a purified preparation of the active material which they have tentatively named aspergillin O (*Lancet* 2:443, 1959). The fungus was grown in the dark for five days in a liquid medium, which after filtration was passed through an anion-exchange resin (IRA-400). After adjusting the pH to 6.8 a crude precipitate of aspergillin O was obtained by adding acetone. Impurities were removed by suspending the precipitate in water and adding a solution of zinc, copper, and cadmium sulfate. Further purification was effected by dialysis against distilled water, and the solution finally lyophilized. Analysis showed that aspergillin O was largely carbohydrate in nature and contained small amounts of inorganic phosphate and nitrogen. Activity experiments showed that the purified material digested heated bovine and human fibrin in quantities as low as 0.1 Gm. Although a strong inhibitor was found in human plasma and serum, the material was effective in lysing human plasma clots, especially if added after the clot had formed. Its activity was enhanced by heparin. On incubation with plasma it showed strong anticoagulant activity. Aspergillin O was used in the control of experimental thromboembolism in dogs and in the treatment of selected cases of the condition in man.

Anthrax.—In a sampling survey of imported hides in Liverpool Semple and Hobday found that a high proportion were contaminated with Bacillus anthrax spores (*Lancet* 2:507, 1959). The extent of contamination depended on the country of origin, the hides from Argentinian cattle showing the lowest infection rate (3%), and those from West African the highest (64%). It is likely that about 25% of the hides imported into Britain are contaminated with the spores of B. anthrax. Commercial grading of the hides does not seem to influence the infection rate. In spite of this, anthrax is rare among those who handle the hides. The survey was made in Liverpool, where only seven cases of anthrax were reported in the last five years. Normally the immunity against anthrax must therefore be high. Even so, they consider it worth while to immunize all those, such as dockers and leather process workers, who handle imported hides.

Fibrinolysis.—A new method of determining the fibrinolytic activity of whole blood was devised by Maclagan and co-workers (*Lancet* 2:471, 1959). In an investigation of the possible role of fibrinolysis in the cause of atheroma, preliminary experiments indicated the need for a more accurate method of determining the labile fibrinolytic activity of blood. With the Maclagan technique the rate of lysis is followed by means of hourly estimations of the hemoglobin content of the clot. A graph is then plotted and the time for 50% lysis calculated. Venous blood was found to be satisfactory if collected without stasis, which produces a significant shortage of lysis time. The existence of a diurnal variation in lysis time was confirmed by a study of 53 subjects, but this diurnal variation occurred only if they were ambulant. Subjects confined to bed showed no such variation. A significant inhibition of lysis time occurred within two hours of consuming a meal containing 1½ oz. of butter. There was a correlation between the degree of lipemia, as measured by plasma turbidity, and inhibition of lysis.

Moderate exercise greatly accelerated fibrinolysis. The effect of this was transient and disappeared within 90 minutes. It was able to overcome the inhibiting effect of large quantities of butter in the diet. The combined effects of inactivity and eating a large quantity of unsaturated fat were particularly impressive, producing about double the active control lysis times. The results were consistent with the current speculations on the effects of dietary fat in promoting, and of exercise in limiting, the development of atheroma.

Cost of Medical Care.—An investigation on national expenditure on medical care was made by J. R. Seale, who studied first hand the working of the medical services in both Britain and the United States (*Lancet* 2:555,1959). He stated that national expenditure on medical care is broadly related to the national income of the country concerned and tends to remain fairly constant in spite of economic setbacks due to recessions and wars. In the last 28 years the proportion of gross national income devoted to medical care has fluctuated between 3 and 4.5% in the United States. During the depression of the early 1930's the proportion spent was greater than it is today. It sank to about 3% in World War II.

Two conflicting groups of forces act on national expenditure on medical care. Medical, social, economic, and political sources that tend to push expenditures upward are balanced by limitation of private funds which prevents expenditure rising above a certain level. It is often thought that advances in medicine will result in the prevention of disease, a healthier population, and therefore less expenditure on medical care. While it is true that the eradication or speedy cure of many infectious diseases in the wealthier countries has occurred, this has lengthened the life span, and neoplastic and degenerative diseases have increased in consequence. These are more costly to treat. Advances in medical diagnosis and treatment have merely altered the pattern of disease. The application of new medical techniques and methods of diagnosis is increasing the cost of medical care.

As the standards of living increase more money will be spent on the hospital services. The citizens of a wealthy country expect to eat better, have more luxurious hospitals, better laboratory and diagnostic facilities, more nurses, improved operations, and better preoperative and postoperative care. Rising wages leave more money for medical care. In a modern democracy the pressures on politicians to spend public funds on medical services are strong and promises in this direction provide bait for votes in political elections, but in a nationalized health service expenditure on medical care is subservient to the demands of national defense, unemployment and old age insurance, and public utilities. A high standard of medical care provided by the state means high taxation, which is unacceptable to the public. A nation cannot have all the medical care it needs but only what it can afford or is willing to pay for. This, in practice, like expenditures for food, clothing, and housing, is a fairly constant proportion of the national income.

From a study of American statistics Seale submits the following propositions: 1. The proportion of the gross national wealth of a nation devoted to medical care tends to remain constant. 2. It rises during national economic depressions and it falls during wars, because the proportion spent on medical care is constant, and in depressions the national income falls, while during wars it becomes artificially inflated. 3. A persistent rise in real per capita gross national income will tend to result in a gradual increase in the proportion spent on health.

Parathion Poisoning.—A child was admitted to the Civil General Hospital, Singapore, with abdominal pain and vomiting. Within six hours nine more children were hospitalized for the same reason. All were seriously ill, and two died. Poisoning with an anticholinesterase was suspected and barley-water, which is a popular drink with children in this region, was finally found to be the source. More children were affected later and eight died, all from what appeared to be the same cause. The children became ill two or three hours after drinking barley-water, and rapidly became prostrate, then comatose. Excessive salivation was followed by pulmonary edema within a few hours. Large doses of atropine produced improvement. The severity of the symptoms was related to the amount of barley-water consumed, and the symptoms were worse in those who had eaten barley as well. The source of the barley was traced and it was found to be heavily contaminated with parathion, an anticholinesterase insecticide of the phosphorus type. Contamination occurred during shipment of the grain, which was stored in the same hold as the insecticide.

Cerebral Demyelinization.—Two groups of workers have drawn attention to an unusual neurological complication of disorders of the reticuloendothelial system, consisting of widespread, often confluent, foci of demyelinization in the brain, with changes in the neuroglial cells. Cavanagh and co-workers and Lloyd and Urich described patients who had Hodgkin's disease and lymphosarcoma with these neurological complications (*Lancet* 2:524-529, 1959). All patients developed an illness that progressed rapidly and without remission and finally proved fatal. Before death clinical evidence of widespread bilateral cerebral damage was evident, dementia and pyramidal-tract lesions being the presenting symptoms in the patients with Hodgkin's disease. Homonymous hemianopia, body-image disturbance, hemianesthesia, and bulbar palsy were other notable symptoms. A patient with lymphosarcoma suffered from headaches, unilateral paresthesia, diminished vibration sense, impaired vision, and internal ear deafness.

At autopsy distinct pathological lesions were found in the brain, which were not due to infarcts from infiltration with leukemic or reticulosis deposits. The astrocytes were hyperplastic and showed gross enlargement of the nuclei, with increased affinity for stains, and mitotic figures in prophase and metaphase. It was suggested that a disturbance in normal immune mechanisms might be a factor in the production of the cerebral lesions in these patients. Another possibility is a metabolic disturbance involving lipid metabolism, particularly that of sphingomyelin.

eaths from Poisoning.—In the last year there ere 1,188 deaths from poisoning in Great Britain, 35 of them suicidal and 353 accidental. Although ore men than women committed suicide, self-estruction by poisoning occurred oftener in women 56 women and 379 men). This was undoubtedly ue to the larger number of women having access aspirin and barbiturates for medical reasons. Both en and women used these drugs more than any thers for suicidal purposes. Aspirin was taken by bout 20% and barbiturates by just over 65% of ose committing suicide by drugs. Other drugs used ere mainly sleeping tablets, antihistaminics, and licylates. The chemicals most frequently employed suicides were cyanide, a mixed phenol preparaon (Lysol), hydrochloric acid, ammonia, and niconе in order of frequency. There were three suiides from insulin overdosage and three from taking trychnine.

The distribution of deaths from accidental poisonng by drugs and chemicals was equal among males nd females. Here again the commonest causes ere an overdose of barbiturates (59%) or aspirin 9%). Other substances causing accidental deaths ere analgesic and soporific drugs, alcohol, and ndustrial solvents. Twelve children under 5 years f age died from aspirin and salicylate poisoning nd four from strychnine poisoning.

mall Babies for Mothers Who Smoke.—Women who smoke have much smaller babies than do nonsmokers, according to a report in the *British Medical Journal* of Oct. 10. These findings were made in an investigation into the effect of smoking on the pregnancies of more than 2,000 women in six Birmingham hospitals. It was directed by Dr. C. R. Lowe. The infants of mothers who smoked throughout pregnancy weighed on the average 6 oz. less than those of mothers who did not smoke. This could not be attributed to sex difference or a difference between the birth weights of first and later births. Furthermore it was great enough to lower significantly the incidence of surgical induction of labor among smokers. The mean weight of infants of those who smoked 10 or more cigarettes a day was less than that of infants of women who smoked fewer than 10 cigarettes a day. Male infants of regular smokers were appreciably lighter than female infants of nonsmokers, a reversal of the usual sex difference in weight. There was no evidence that the low birth weight of infants of women who smoked was due to shortening of the period of gestation. Smoking adversely affects appetite, and it was found that smokers weighed significantly less than nonsmokers, but the difference hardly seemed sufficient to account for the difference in birth weight, since dietary deficiencies had little influence on birth weight unless they were severe.

This view was supported by the observation that when the mothers were grouped according to their weights the infants of nonsmokers were heavier than the infants of smokers for each maternal weight group. The effect of smoking was unrelated to maternal age or to the number of children a woman had had. There was nothing to suggest that cigarette smoking was related to complications of pregnancy. It was therefore concluded that smoking during pregnancy substantially retarded fetal growth. It might be that tobacco had a direct pharmacological action on the fetus, since the fetal heart rate increased when a pregnant woman smoked a cigarette. An even more credible explanation was that smoking limited the blood supply to the fetus.

Safer Surgery.—Smylie and co-workers of the Aberdeen Royal Infirmary (*British Medical Journal*, Oct. 3, 1959) reported that widespread concern about cross-infection in surgical wards has led to a more precise reevaluation of many aseptic techniques. The need for an improved surgical scrubbing became apparent during an investigation into sepsis rates in two surgical units in this hospital. Because the most troublesome of hospital pathogens, Staphylococcus aureus, is resistant to ordinary cake soap, an experiment was made with a soapless detergent cream incorporating 3% hexachlorophene, with a pH of 5.5 (that of the skin). This water-miscible anionic detergent cream, pHisoderm, contains a sulfonated ether, wool fat, cholesterols, and petrolatum, and is a surface tension reducent 40% more powerful than soap. The remarkable effectiveness of hexachlorophene as a skin disinfectant is well recognized. A detergent-disinfectant combination, pHisoHex, compares favorably with other detergents and antibacterial agents. The scrubbing time of only three minutes with it brought some criticism from the surgical staff, but the bacteriological results showed it to be far more effective than soap in the circumstances of this trial. The amount of suds produced was a little less than with soap, and this again caused some criticism. Although a powerful disinfectant, hexachlorophene does not disinfect the skin as quickly as does 70% alcohol. Consequently the bactericidal effect of pHisoHex can be attributed to the efficient deposition of hexachlorophene as a semipermanent film on the skin of frequent users. The result, which was controlled by the use of culture mediums inhibitory to pHisoHex, showed that the new method produced a highly significant fall in the number of colonies of skin organisms grown from the finger pads of the surgical team at the end of operations.

Remuneration in the National Health Service.—With the approval of the British Medical Association, Brotherston and co-workers of the Department of Public Health and Social Medicine, University of Edinburgh, conducted an inquiry among Scottish physicians to obtain their views on alternative systems to the one in use for paying general practitioners in the National Health Service (NHS). At present the method of payment is on an annual per capita basis, which is independent of the number of patients seen or of the amount of work done by the doctor. Half the Scottish general practitioners were sent a questionnaire and nearly 80% replied. Only 2% were in favor of retaining the present system. About 12.5% thought that payment by salary was the most suitable for general application, and about 17% preferred it to be based on fees for service. Apart from 5% who suggested various combinations of these methods, about 65.5% wished to have a modified form of the present per capita system.

The doctors were asked to name the factors that should be taken into consideration in arriving at their remuneration. Very few thought that the number of patients on a doctor's list should be the only factor in determining his income, as in the present scheme. Most of them thought that the number of consultations should be taken into consideration, although they did not favor a straight fee-for-service method of computing remuneration. Another important factor mentioned was length of experience. Most thought that a general practitioner's ability and knowledge largely depends on the experience he has had and that this should be suitably rewarded. At present a newly qualified general practitioner receives the same capitation fee as his senior colleague of 20 or more years' experience.

The capitation system was generally condemned as it was thought to encourage the indiscriminate hunting for patients, or "head hunting" as it has been called, with resulting deterioration in standards of practice and undignified competition with colleagues. Payment of a fee for service was believed to involve too much clerical work (although it is done by dentists in the NHS) and to lead to overtreatment and possibly abuse. A salaried service was condemned as it would fail to relate income to ability or conscientiousness and would probably lead to loss of professional freedom.

Asked how the present system of payment could be improved, most general practitioners were in favor of reducing the maximum size of the existing list of 3,500. The alternative maximum commonly suggested was 2,500. Increased payments for maternity services, the abolition of grants for training assistants, increased supplementary payments and mileage allowances on cars, and changes in the loading system designed to discourage large lists were other recommendations mentioned.

Tolbutamide.—Loubatière's original hypothesis that the sulfonylureas lower the blood sugar level by stimulating endogenous insulin production has not been finally accepted because these drugs do not reproduce all the metabolic effects of large injections of insulin. To elucidate the mode of action of tolbutamide, Russell Fraser and co-workers estimated the plasma insulin level in normal subjects and diabetics before and after the administration of this drug. Plasma insulin activity was measured by its effect on the glucose uptake of the rat diaphragm. Tolbutamide itself neither increased the glucose uptake of the rat diaphragm used in insulin assay nor enhanced the effect of insulin. It can, therefore, be assumed that it does not lower the blood sugar level in the body by potentiating existing insulin. The blood sugar and plasma insulin activity were measured in five normal subjects and 22 diabetics before, and two and one-half hours after, giving 2 Gm. of tolbutamide. The latter were graded according to the clinical response obtained. The plasma insulin level rose in the normal subjects and in the clinically responsive diabetics but not in those who did not respond. The fall in blood sugar level correlated with this rise in plasma insulin activity. These results suggest that tolbutamide lowers the blood sugar level by stimulating endogenous insulin production, provided there is an adequate pancreatic reserve of insulin.

These authors also showed that single-dose tests of the hypoglycemic action of tolbutamide give only an approximate prediction of the long-term clinical control that is likely to be obtained. These tests can distinguish between those diabetics who do not respond and most of those who will show some persistent response, but they do not distinguish between those whose symptoms will be satisfactorily controlled and those whose response will be only fair. The difference between these good and fair responders probably depends on the adequacy of their insulin reserves. When the reserve is small, a single dose of tolbutamide may cause an impressive response, but a larger reserve is doubtless required for a sustained response to regular daily stimulation.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Ischaemic Electrocardiograms in Symptomless Men with a Note on the Serum Lipoproteins. D. Weitzman and E. B. Smith. Brit. M. J. 2:162-166 (Aug. 15) 1959 [London].

The authors obtained electrocardiograms from 100 hospitalized men, between the ages of 50 and 80 years, none of whom had chest pain or any evidence of cardiac disease. Abnormal tracings showing evidence of myocardial ischemia were recorded for 12 of these men. Thirty-five of the 100 patients died as a result of the illness which occasioned their admission to St. Bartholomew's Hospital in London, and autopsy was performed on 19. From 6 of the 19 patients abnormal electrocardiographic tracings suggesting myocardial ischemia had been obtained, but in all 19 the absence of any cardiac lesion, other than coronary atheroma, was confirmed by autopsy. In 12 patients, including 3 with ischemic electrocardiographic tracings, the coronary arteries were examined roentgenographically. A normal vascular pattern was observed in the roentgenograms of 6 patients from whom normal electrocardiographic tracings had been obtained. An increased anastomotic pattern, with a subendocardial plexus indicative of ischemia, was observed in the roentgenograms of the remaining 6 patients, 3 of whom had ischemic electrocardiographic tracings; in these latter 3 the anastomotic network was particularly dense. These findings emphasize the need for care in using electrocardiography in the assessment of chest pain, which is not necessarily of cardiac origin even though the tracing be abnormal.

In 59 of the 100 men, including 9 of the 12 with abnormal electrocardiographic tracings, the serum lipoproteins were examined by paper electrophoresis for the presence of an abnormal pre-beta-lipid band that is roughly equivalent to the molecular species S_f 20 to 100 undergoing flotation in the ultracentrifuge cell, as reported by Gofman and co-workers. The lipoprotein findings were compared with those in a group of 71 men with ischemic heart disease. A moderate quantity of abnormal lipid was found in a similar percentage of both groups and did not correlate with clinical coronary disease. A large pre-beta-lipid band did, however, appear to correlate with electrocardiographic evidence of myocardial ischemia.

Pulmonary Embolism and Infarction (with a Review of Cases at San Patricio V. A. Hospital). F. A. Poueymirou, E. A. R. Rodriguez and A. F. de Juan. Bol. Asoc. méd. Puerto Rico 51:259-267 (Aug.) 1959 (In English) [Santurce].

Forty cases of pulmonary embolism observed between 1947 and 1958 at the San Patricio Veterans Administration Hospital in Santurce, Puerto Rico, are reviewed. Inclusion of each case in this study was determined by one or all of the following criteria: a clinical picture with compatible electrocardiographic and/or radiologic findings; electrocardiographic pattern of acute cor pulmonale unattributable to any other condition; and the finding of either an infarcted lung area or of a pulmonary artery occlusion at autopsy. The mean age of the patients at the time the embolism occurred was 44 years; the youngest was 20, the oldest was 68. In all 40 cases the condition was traced to thrombotic embolism. In 25 patients (63%) there was evidence of significant heart disease on admission to the hospital. The condition most frequently present at the occurrence of the attacks was heart failure in 18 patients, malignant tumor in 8, fibrillation in 5, and recent myocardial infarction in 4. Fifteen of the patients in this series recovered. Autopsy findings in 25 patients indicated that pulmonary embolism had been the cause of death in 7 patients and a contributory factor in 14; in 4 it was an incidental finding.

Acute pulmonary embolism was silent in several of the patients studied. Of the 50 attacks which occurred among the 40 patients, 25 were followed electrocardiographically. In some cases the electrocardiographic tracings were not obtained immediately after the embolization, because the possibility of this diagnosis had not occurred to the physicians in charge. Only the acute cor pulmonale pattern is clearly conducive to the diagnosis of pulmonary embolism, but the complete pattern is rare and occurred in only one patient in this series. The authors emphasize that pulmonary embolism is the most frequent complication detected in hospitals. Effective means are available

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for treating and preventing this complication if the condition is recognized or suspected early. The degree of awareness of a possible pulmonary embolism must be increased in order to use effectively the diagnostic help of electrocardiography, and to interpret properly the laboratory and x-ray findings. The absence of an immediately apparent site of thrombosis does not exclude the diagnosis of pulmonary embolism. Although both surgical and medical conditions may be associated with pulmonary embolism, in the present study the number of patients under medical treatment (33) was much higher than the number of those (7) in the postoperative stage.

Chronic Cor Pulmonale Following Thromboembolism: A Clinical and Pathophysiological Study of Three Cases. L. Ehrner, T. Garlind and H. Linderholm. Acta med. scandinav. 164:279-297 (no. 4) 1959 (In English) [Stockholm].

The authors report on 3 men, aged 43, 30, and 43 years, respectively, with chronic cor pulmonale occurring after thromboembolism of the pulmonary artery. The first of these 3 patients had signs of superficial thrombophlebitis at about 25 years of age and 4 years later probably had a pulmonary embolism. He then remained free of symptoms for 5 years, but he had repeated attacks of bronchitis, and symptoms of asthmatic type occurred. Seven years later heart failure supervened. Heart catheterization revealed pulmonary hypertension, and angiocardiography showed partial occlusion of the main branches of the pulmonary artery. The patient died, and at autopsy the clinical diagnosis of massive thromboembolism was confirmed. No sources of embolism could be found. The second patient, an athlete cyclist, was healthy until the age of 23 years when he had bilateral pleurisy and parenchymal infiltrations of unknown causation. Three years later he had a thrombosis of the right leg. After another 3 years he suddenly became dyspneic and had signs of thrombosis in the left leg. Afterwards he was completely disabled. On 2 occasions chest roentgenograms showed thin-walled cavities in the right lung associated with fever and hemoptysis. He became psychotic and died. Autopsy confirmed the clinical diagnosis of pulmonary embolism with subsequent chronic cor pulmonale. There were large organized thrombi in both branches of the pulmonary artery and a persistent foramen ovale. The third patient had symptoms of bronchial asthma at the age of 34 years. Three years later he had on 2 occasions thrombosis of the legs and an attack of unconsciousness probably due to pulmonary embolism. Soon after that he had a massive hemoptysis. On repeated occasions thereafter he had infections of a bronchopneumonic type with infiltrations into the upper lobes, in which big cavities arose. He also had chronic sinusitis. His asthmatic complaints have diminished during late years, but his dyspnea has increased, and he is at present considerably disabled.

The thromboembolic disease thus started rather suddenly in fully active, apparently healthy young men. The duration of symptoms varied between 2 and 14 years. The physiological examination revealed a low exercise tolerance; pulmonary function tests revealed normal conditions, including a fairly normal diffusing capacity of the lungs. There was an increased venous admixture in all 3 patients. In one patient at least part of the shunted blood might have passed through a persistent foramen ovale. During work the breathing rate was high at a comparatively low pulse rate. Ventilation and alveolar ventilation were excessive at rest and also during work. A considerably raised vascular resistance of the lesser circulation, resulting in a strain on the right heart, was a common finding in all 3 patients. The stroke volume was low in 2 patients at rest and decreased during work in the third. The cardiac output was low in relation to oxygen uptake in the 2 patients with the severest disease.

The diagnosis of chronic cor pulmonale after thromboembolism of the pulmonary artery should be suspected in patients with dyspnea and normal results of pulmonary function tests and no signs of primary heart disease, particularly if there is a history of peripheral thrombosis. Orthopnea seems to be a late symptom which occurs only when heart failure supervenes. Diagnosis is aided by a typical roentgen-ray picture with centrally dilated and peripherally thin pulmonary vessels, electrocardiographic signs of right ventricular strain, and a high pulmonary vascular resistance shown by heart catheterization. Angiocardiography may confirm the diagnosis.

The Ultimate Fate of Calcified Tuberculous Focus in Children and Adolescents. H. D. Renovanz. Tuberkulosearzt 13:519-528 (Aug.) 1959 (In German) [Stuttgart, Germany].

Calcification of tuberculous foci was found in 532 of 5,216 children who underwent treatment at the Sanatorium Aprath, in the Rheinland, Germany, from 1954 to 1958. The average interval between the first radiologic manifestations of tuberculosis and radiologic evidence of calcification was 11.2 months for children under 2 years of age, and 19 to 22 months in older children. Resolution of the calcified lesions, partly by absorption and partly by softening, followed by expectoration of the caseated mass via the supplying bronchus, was observed in 1.8% of the patients. Exacerbation of the tuberculous process was observed in 13% of the children with calcified lesions. In 17% of these patients exacerbation was associated with cavitation. A comparison of these figures with those calculated for adults shows that the risk of calcified foci becoming active and undergoing cavitation increases after puberty. The observations made in these patients indicate that a calcified focus does not invariably represent the last stage in the course of the tuberculous disease. A calcified focus often constitutes a reservoir of tubercle bacilli which may suddenly resume growth and cause reactivation of the tuberculous process.

Lymphocytic Leukemia: Symptomatology and Results of Therapy in 160 Cases. L. Heilmeyer, G. Mössner and K. Hess. Klin. Wchnschr. 37:790-794 (Aug. 1) 1959 (In German) [Berlin].

The authors report on 125 men and 35 women with lymphocytic leukemia, who were admitted to the medical clinic of the University of Freiburg im Breisgau, Germany, between 1945 and 1957. Sixty-three (39.5%) of the 160 patients were between the ages of 50 and 60 years, 39 (24.4%) were between 60 and 70, and 33 (20.6%) were between 40 and 50. Only 2 patients were aged less than 20 years. The highest incidence of lymphocytic leukemia among those in the 5th decade is statistically significant. On admission, 93 patients (58.1%) had an increased size of the spleen, 97 (60.5%) had generalized enlargement of lymph nodes, 28 (17.5%) had localized enlargement of lymph nodes, 37 (23.1%) had enlargement of mediastinal lymph nodes, and 6 (3.7%) had enlargement of abdominal lymph nodes. Only 20 patients had a rise of temperature in the course of their disease. Sternal puncture was performed in 103 patients and confirmed the diagnosis in 91. Of 39 patients who died at the clinic, autopsy was performed in 16 and confirmed the diagnosis in all.

Of the 160 patients, 13 received roentgen irradiation alone, 53 received cytostatic chemotherapy alone, 68 received combined cytostatic chemotherapy and irradiation therapy, and 26 did not receive any specific treatment. The average survival time of the 160 patients was 3 years and 10 months. The best results were obtained in patients who received roentgenotherapy alone, with an average survival time of 4½ years. Next in order were the results obtained in patients without specific therapy, who received only cortisone and arsenics; the average survival time of these patients was 4 years and 4 months. The least satisfactory results were obtained in patients who received cytostatic chemotherapy alone and whose average survival time was 3½ years. The average survival time of patients with combined cytostatic chemotherapy and irradiation therapy was 3 years and 10 months. Other workers also reported an average survival time of 3 years and 10 months as compared with the best survival time of 4½ years observed by the authors. Triethylene melamine (TEM) was the cytostatic chemotherapeutic agent used in most of the patients. Remissions were highest among patients receiving roentgen irradiation therapy alone; next in order were remissions occurring among patients with combined chemotherapy and roentgen irradiation therapy; and the lowest incidence of remissions was observed among patients who received chemotherapy alone.

It is not easy to evaluate the reported therapeutic results, because the therapeutic subgroups of patients are too small to be considered statistically significant. Moreover, the therapeutic results depended, at least partly, on a selection of patients, in that the various methods of treatment were practiced according to the patient's general condition and the stage of the disease. In addition, it seems that the conditions inevitably leading to a certain course of lymphocytic leukemia may be inherent from the start in the individual patient and hardly subject to influence by therapy. Although cytostatic chemotherapy alone yielded the worst results, it is a valuable adjunct to treatment, because it may still be practiced with some prospect of success, while other methods, such as roentgen irradiation, would overtask the patient's remaining strength, and because chemotherapy combined with roentgen irradiation may induce a response to the latter in patients whose condition has been refractory to roentgen irradiation.

Pulmonary Disability in the Hurler Syndrome (Lipochondrodystrophy): A Study of Two Cases. J. F. Murray. New England J. Med. 261:378-382 (Aug. 20) 1959 [Boston].

The author reports the occurrence of severe respiratory disability in a 43-year-old man and in a 3-month-old male infant with lipochondrodystrophy (Hurler's disease). The adult patient showed the classic features of lipochondrodystrophy, such as dwarfism with a grotesque physique (kyphoscoliosis), limitation of joint motion, deafness, hepatosplenomegaly, hernia, and probable cardiac involvement. The infant lacked the skeletal deformities but had corneal clouding and mental retardation. This patient died at the age of 16 months, and death resulted from acute bronchitis with bronchopneumonia. Autopsy revealed overaerated lungs with focal areas of atelectasis; Adler bodies were observed in the leukocytes, and intracellular storage of an abnormal material was found on microscopic examination. In the adult the disease became manifest in early childhood, and in the infant it was manifest at birth. Pulmonary function studies in the adult patient through a tracheostomy tube, which had been inserted for "acromegaly of the larynx" 7 years before the patient's admission to the Los Angeles Medical Center, revealed a reduced vital capacity and an increased residual volume. Obstruction of the upper airway is a characteristic feature of lipochondrodystrophy, and both patients had mouth breathing, nasal congestion, and rhinorrhea. Both patients had repeated episodes of respiratory infection. Respiratory disability is one of the most important aspects of lipochondrodystrophy. Upper-airway obstruction, kyphoscoliosis, restricted chest motion, and chronic respiratory infections are common features of the disease, so that tracheostomy, which may benefit all these disabilities, should be considered early in the course of the illness.

Present-day Treatment of Hemophilia. R. Masure. Acta clin. belg. 14:152-161 (March-April) 1959 (In French) [Brussels].

The treatment of hemophilia, which is limited at present to the prevention and cure of hemorrhage, brings up problems of local and, more especially, general hemostasis. Many direct methods of influencing blood coagulation have been tried and abandoned. Corticotherapy is the only general medicamental treatment that deserves a trial; used as an adjuvant, it may act in a nonspecific manner on capillary resistance in certain cases of subacute hemarthrosis, hematuria, or edema superimposed on hematoma, but its results are inconstant. The basic treatment for hemophilia still remains the transfusion of blood or its derivatives, because transfusion is the only method of correcting the coagulation defect by supplying the missing factor or factors. The only forms of hemophilia that need to be considered in practice are hemophilia A, hemophilia B, angiohemophilia, and hemophilia with circulating anticoagulants. Fresh whole blood, blood stored at 4 C under the usual blood bank conditions, fresh plasma kept frozen at —30 C, and irradiated and lyophilized plasma may be used in various types of hemophilia. Dried antihemophilic globulin and fresh Cohn fraction 1 are useful only in hemophilia A (classical hemophilia) or angiohemophilia (von Willebrand type). Hemophilia B (Christmas disease) responds to stored blood, standard dried plasma, or fraction PPBS, which combines prothrombin, proconvertin, antihemophilic factor B, and the Stuart factor, that is, all the factors depressed in the course of anticoagulant therapy with coumarin and its derivatives. The concentrated fractions are intended essentially for the treatment of cases refractory to the standard therapy with blood or plasma.

The amounts to be transfused to secure hemostasis will depend on the level of antihemophilic factor present in the patient's blood, on the existence or not of a refractory state (circulating anticoagulants), and on the extent of the trauma. The level of the antihemophilic factor necessary for hemostasis may have to be raised to 20, 30, or even 50% in patients who have suffered severe trauma or who are to undergo surgical procedures; consequently, the corrective power of normal plasma should always be tested by adding it to the patient's plasma in various proportions and observing the resulting recalcification and prothrombin consumption times. Antihemophilic factor A disappears from the circulation in less than 24 hours; factor B, in from 10 to 20 days. Transfusions, when needed, should therefore be given every 6 to 12 hours to patients with a deficiency of factor A and every 4 days to those lacking in factor B. Treatment with transfusions should be continued for 3 or 4 days when dental operations are to be performed, and for 8 to 10 days when the operations are more extensive. Transfusions for reasons other than severe hemorrhage and surgical operations should be avoided as much as possible in order to prevent the development of a refractory state associated with the production of circulating anticoagulants acting against the antihemophilic factors. The appearance of these inhibitors greatly aggravates the prognosis and often necessitates the administration of the concentrated fractions.

Carefully applied local treatment will usually make transfusions unnecessary, and so most of the sequelae will be prevented. Prolonged gentle pressure should be applied over wide area by means of lastex bands, or, in the case of epistaxis, by absorbable tampons of gelatin impregnated with thrombin. Punctures and injections should be avoided in patients with hemarthrosis, except when the distention of the joint is extreme. Every effort must be made to prevent trauma, however slight. Children, in particular, should be carefully watched and taught to avoid injury.

Further Experiences with Severe Allergic Reactions to Insect Stings. H. L. Mueller. New England J. Med. 261:374-377 (Aug. 20) 1959 [Boston].

The author reports on 57 male and 27 female patients, between the ages of 3 and 56 years, who had systemic reactions to stings of bees and wasps. Of the 84 patients, 12 had slight general reactions, 36 had general reactions, 23 had severe general reactions, and 13 had shock reactions. The more rapid the onset of symptoms after the sting, the more severe the reaction was likely to be. Sixty-three (75%) of the 84 patients had a family history of allergy, and 28 of these had a personal history of other allergy as well; these 63 patients had a tendency to have more severe reactions than the 21 who had no family or personal history of other allergy. Six of the 84 patients were not treated for various personal and economic reasons. Seventy-eight patients were treated, but 2 of these did not return for treatment. Of the 76 patients with continuing treatment, 13 have completed 3 years of perennial inoculations with a mixed whole-insect extract of equal parts of bee, wasp, hornet, and yellow jacket. The starting point in dilution for treatment with this polyvalent insect extract varied from 1:100,000,000 to 1:1000. The remaining 63 patients are still receiving maintenance doses of the polyvalent insect extract. Of the 76 patients, 30 (about 40%) have had a total of 48 stings after treatment was started. With one exception, all the patients who have been stung while on a maintenance dose of 0.15 cc. or greater of a 1:100 dilution of the polyvalent insect extract, or who have been stung after completing 3 years of treatment, have had no resulting systemic symptoms.

Severe reactions to insect stings occur more commonly than is generally supposed, and it is possible that unrecognized cases account for some of the sudden deaths attributed to heart failure and heat prostration in the insect seasons. Identification of the insect causing the sting reaction is unreliable, unless the insect is captured and identified by an expert. Intracutaneous testing reveals that extreme sensitivity may occur in these patients, that multiple sensitivity is usually present, and that these tests, in general, can be used as a guide for starting doses in treatment. In all patients who have had a systemic reaction to a sting by a bee, wasp, hornet, or yellow jacket, treatment with a mixed whole-insect extract of these 4 types of insects is advised, starting with the dilution that gives the "initial positive test," and increasing gradually to a maintenance dose of 0.2 to 0.3 cc. of 1:100 dilution. If testing is not performed, it is recommended that patients be started at 0.05 cc. of a dilution of 1:100,000,000.

The Painful Reaction to Alcohol in Hodgkin's Disease. V. Giuliani and M. Talarico. Riforma med. 73:876-880 (Aug. 1) 1959 (In Italian) [Naples].

The authors report on the reaction to the alcohol test in 16 patients (11 male and 5 female ranging in age from 25 to 39 years) with malignant lymphogranuloma (Hodgkin's Disease), in 6 patients with various types of lymph node involvement, and in 5 normal individuals. The disease was in the active stage in 10 of the 16 patients with lymphogranuloma and stationary in the other 6. These latter patients had been treated with nitrogen mustard or irradiation therapy; the other 10 had received no treatment. Of the patients with lymphogranuloma, alcohol was given orally to 4, intravenously to 8, and orally and intravenously to the remaining 4. Pain developed in 3 of the 10 patients with the disease in an active stage. There were no positive results among the patients with lymph node involvement other than those in Hodgkin's disease. Therapeutic treatment, followed by a remission of the disease, had a marked effect on the results of the tests, which became negative when the disease became stabilized. Vasodilator preparations, given orally or topically, had no effect on the pain induced by the alcohol. The results of the test were not influenced by the administration of tetraethylthiuram disulfide. Differences in the way in which the alcohol was administered did not greatly affect the results; the authors, however, believe that the intravenous administration is preferable. The pain appeared immediately, especially in patients who received the alcohol intravenously, lasted for from 30 to 40 minutes, and usually passed away spontaneously. Involvement of the lymph nodes of the area in which the pain occurred was not observed, although during and after the test the nodes were more perceptible on palpation. The authors believe that the accumulation in the lymphogranulomatous tissue is not due to a local vasodilation, but to a depolymerization of the chemical constituents of the intercellular substance of the tissue, especially in the hyaline-fibrous part of the sclerotic zones which are very extended. Because of the low percentage of positive reactions, the authors believe that the test, though specific, is not pathognomonic of malignant lymphogranuloma.

Treatment of Severe Tetanus. J. R. Lawrence and M. J. W. Sando. Brit. M. J. 2:113-118 (Aug. 1) 1959 [London].

The authors report on 9 patients with severe tetanus, who were observed from June to October, 1957, at the Royal Adelaide Hospital and who were treated by the administration of doses of tubocurarine sufficient to paralyze the voluntary muscles and by artificial respiration. Each patient was first given 300,000 units of antitetanic serum, half of it intravenously. Tracheostomy was performed under general anesthesia, when it was indicated. At the same time débridement of the entry wound was performed when necessary, and a cuffed rubber tube was inserted. A "polythene" catheter was introduced to administer nourishment and drugs by intravenous drip. The earlier patients received mephenesin, and the later ones chlorpromazine. Penicillin was given, and the sedatives found to be useful were promethazine, pethidine, chlorpromazine, paraldehyde, and chloral. Sterile tracheal toilets were done when tracheostomy was performed.

Curarization was begun with artificial respiration in instances in which heavy sedation failed to inhibit spasms, especially of the muscles of respiration. Curarization was instituted by the intravenous route, but maintenance could be effectively achieved by intramuscular injections of between 60 and 90 mg. of tubocurarine. The indications for further doses were a rising blood pressure or pulse rate, the appearance of muscular twitches, movements of the tongue, face, or lips, or breathing motions. The ideal time for decurarization was when the patient could tolerate tracheal suction and could cough without developing generalized spasms. It was determined by trial. The period required varied from 18 to 72 hours, a careful watch being maintained for evidence of persistent severe tetanic activity.

Four patients died, 2 of them of pulmonary embolism and another in acute renal failure. Several other complications occurred, including hyperglycemia and bone-marrow depression, thought to be related to prolonged nitrous oxide administration. Hyperglycemia in 3 patients was so severe as to warrant the use of insulin. The authors believe that the technique of paralysis and mechanical artificial respiration has a real place in the management of tetanus. It is indicated in the fulminating case or in the severe case when sedation and other relaxant agents fail to control reflex spasms and thoracic rigidity. It should be begun as soon as it is evident that simpler measures will not adequately control the tetanic process.

Essential Hyperlipemia: Review. E. Dollerup and S. E. Jensen. Ugesk. laeger **121**:1151-1159 (July 23) 1959 (In Danish) [Copenhagen].

Of 141 cases of essential hyperlipemia published, only 112, in 17 children and 95 adults, have been described in detail. The disease appears without known causal relation with any other disease and is marked by considerable increase in the neutral fat level of the serum and by milky appearance of the serum in the fasting state. The serum cholesterol and phospholipid concentrations are often increased. While essential hyperlipemia was previously regarded as a benign disease, more recent reports of accompanying grave vascular symptoms have altered this conception. Essential cholesterolemia is distinguished from essential hyperlipemia in that the fasting serum is clear and there is no, or only moderate, increase in the serum neutral fat value. Some cases of essential hyperlipemia are asymptomatic and are recognized only through accidental observation of the lactescent serum. The clinical picture is most frequently described as a triad, consisting of (1) cutaneous xanthomas, (2) attacks of abdominal pain, and (3) hepatosplenomegaly. The cause of the disease is not known. In some cases low-fat diet seems to be effective; in other cases dietetic treatment is without special value, and heparin effects only a slight passing reduction in the serum lipids. Clinically, some cases have several symptoms in common with essential hypercholesterolemia, and a transition form may be considered. The disease occurs at all ages, is most frequent in males, and there may apparently be familial occurrence.

Toxic Megacolon in Ulcerative Colitis. J. L. A. Roth, A. Valdes-Dapena, G. N. Stein and H. L. Bockus. Gastroenterology 37:239-255 (Sept.) 1959 [Baltimore].

The authors report on the occurrence of 15 attacks of toxic megacolon in 12 patients with ulcerative colitis, who were studied on the gastrointestinal service of the Graduate Hospital of the University of Pennsylvania, in Philadelphia, between 1943 and 1958. There were 8 men and 4 women, ranging in age from 20 to 66 years. The term "toxic megacolon" has been used to describe extreme dilatation of a segment of the colon or of the entire colon, which occurred in all these patients during a fulminating first attack of ulcerative colitis, an acute fulminating relapse of the relapsing-remitting type of the disease, or a fulminating exacerbation of the chronic, continuous course of the disease. It was noted in most patients in whom the ulcerative colitis was initially localized to the descending colon or in whom it involved the entire colon or a regional segment. No instances of toxic megacolon were observed in patients in whom the disease was initially limited to the rectum or the rectosigmoid, or in those with enterocolitis (regional stenosing enteritis, usually involving the terminal ileum, in association with ulcerative colitis).

Toxic megacolon may occur as a complication very early or very late in the course of ulcerative colitis. The colonic changes may be reversible, with the colon returning to normal caliber between recurrences of the marked dilatation. A narrowed, apparently stiffened portion of the colon may dilate to 3 or 4 times the normal caliber with a subsequent attack. The clinical configuration of toxic colon in these patients suggested almost complete colonic obstruction with impending perforation. The abdomen was rotundly protuberant, with extreme distention of the colon with gas. Although bowel sounds were usually present, the abdomen was quiescent, with infrequent and feeble peristaltic activity. The transverse colon was dilated in all the patients, and was the site of maximal dilatation in most. The average diameter of the colon during the phase of toxic dilatation was 9 cm., as revealed by the roentgenogram. Profound toxicity was a constant accompaniment, manifested by a septic spiking fever, drawn facies, tachycardia, extreme lethargy, and high degree of leukocytosis, with toxic granules and left shift to immature forms of neutrophils. Striking abnormalities of sensorium or mental behavior were noted in most of the patients; these abnormalities included anxiety, profound depression, hysterical behavior, a state resembling parkinsonism, and extreme listlessness. Severe nutritional deficits with low hemoglobin values, hypoalbuminemia, and hypoprothrombinemia were observed, but hypopotassemia was usually not present.

The complications of free perforation, thrombophlebitis, and liver disease were observed more frequently in the 12 patients in whom toxic megacolon occurred during a fulminating attack of ulcerative colitis than in a group of 10 patients with a fulminating first attack of ulcerative colitis reported on by other workers. Two of the 12 patients had fatty liver (as revealed by autopsy), and 3 had moderate Bromsulphalein retention. The duration of the marked colonic dilatation varied from 5 days to 2 months (average, 12.7 days). The termination of the dilatation was abrupt in 9 of the attacks—with 3 patients undergoing an emergency operation for impending perforation, with remission shortly after the institution of corticotropin therapy in 2 patients, with spontaneous remission in 3 patients, and with death in 1 patient. Dilatation of the colon subsided gradually in 6 attacks of toxic megacolon—spontaneously in 3 and after corticotropin therapy in the other 3.

Overwhelming toxemia is probably responsible for the extreme dilatation of the colon through inflammatory degenerative changes or acute necrotic destruction of the muscle fibers or myenteric plexuses, or both. Aerophagy may contribute to the pathogenesis of this dilatation as well as antecedent distal stenosis (without actual obstruction) in some patients. Therapy must be intensive and comprehensive with putting the intestines at complete rest, nothing being administered by mouth during this acute toxic phase. Treatment should include intubation and continuous suction and the administration of antibiotics, blood or protein or both, vitamins B, C, and K, electrolytes (potassium), oxygen, and possibly adrenal steroids. The need for emergency ileostomy and subtotal colectomy should be considered. Six of the 12 patients were treated only with medical measures, with 1 death; surgical intervention was required in the management of the other 6 patients, with 2 deaths, both after emergency subtotal colectomy and ileostomy.

SURGERY

Cancer of the Lung in Tuberculous Patients. N. C. Hamel, J. N. Briggs and L. G. Ludington. California Med. 91:131-133 (Sept.) 1959 [San Francisco].

The records of 7,680 tuberculous patients admitted during a 5-year period to Olive View (Calif.) Sanatorium showed that 4,010 were over the age of 45 years, and that 54 (1.4%) of these had both cancer of the lung and tuberculosis. Not one of the patients with tuberculosis whose age was less than 45 years had this complication. The incidence of carcinoma of the lung in this series of patients with tuberculosis was estimated to be 8 to 10 times higher than that noted in a comparable segment of the general population. Careful examination of serial roentgenograms in all cases of suspected pulmonary lesions was found to increase diagnostic acuity. Scalene node biopsy, cytological studies, and bronchoscopy were of less diagnostic help. The most effective diagnostic procedure has been early thoracotomy in patients in whom there was a reasonable possibility of carcinoma. Thoracotomy was carried out in 25 of the 54 patients with tuberculosis, and diagnosis of carcinoma of the lung was made at the time of operation in 21 of the 25 patients; all except 4 of these patients were found to have tumors of an epidermoid type. Only 2 of the patients with combined disease were women.

The resection in 12 of the patients was intended to be curative in type. Curative resections were done in a greater proportion of patients with active tuberculosis than in those with inactive tuberculous disease. The authors emphasize that it is easy to overlook the slow progress of malignant disease in a patient who has residual fibronodular tuberculosis. Moreover, close and accurate follow-up is not always available in patients with inactive tuberculosis, whereas almost all patients with active disease are in the sanatorium or under close outside supervision. In 85 cases of carcinoma of the lung in nontuberculous patients observed at Olive View Sanatorium in the 5-year period here reviewed, the operability rate was 24%, as compared with 46% for the 54 patients with both tuberculosis and cancer. Curative resections were made in 12% of the nontuberculous patients with cancer, as compared with 22% in patients who had both cancer and tuberculosis.

Surgical Experiences in the Treatment of Congenital Mitral Stenosis and Mitral Insufficiency. G. W. B. Starkey. J. Thoracic Surg. 38:336-352 (Sept.) 1959 [St. Louis].

The author presents 5 patients (3 girls and 2 boys) with congenital mitral stenosis, who were operated on at the Boston Children's Medical Center. The age range from 2½ to 15 years. The diagnosis was made on the basis of the early age of detection of a mitral diastolic murmur (between the ages of 2 weeks and 14 months in 4 patients and at 5 years in the 5th). These children were very ill and in congestive failure. Severe respiratory infections, underdevelopment, and dyspnea were present in all. Three of the 5 patients had had repeated bouts of syncope, often accompanied by cyanosis. A 4th patient had grand mal seizures, accompanied by cyanosis during crying spells. Hepatomegaly was noted in all 5 patients, splenomegaly in 3. Normal sinus rhythm, an apical diastolic rumbling murmur, loud pulmonic second sound, and P pulmonale were observed in all 5 patients. An apical systolic blowing murmur was found in 3 patients, and right ventricular hypertrophy in 4. X-ray examination showed cardiomegaly in all, with enlargement of the right ventricle, left atrium, and pulmonary artery.

Four of these patients were operated on by the "closed" method, a standard left 4th intercostal space incision being used. There was one death on the 5th postoperative day for reasons that were not clear. The results were excellent in one patient and fair to good in the other 2 survivors of the "closed" method of operation. A 5th patient was operated on by the "open" method with aid of a pump-oxygenator. At the end of the procedure the heart began to fail and could not be resuscitated.

The author cites 2 patients with congenital mitral insufficiency who were operated on within the last year. Neither of these patients represented the commoner types of congenital mitral regurgitation, that is, a cleft mitral septal leaflet associated with an ostium primum or atrioventricular canal, or the rarer absent, or vestigial, posterolateral mitral leaflet. These 2 children, like the 5 previously described with congenital mitral stenosis, were very ill and were doing poorly on a medical program. One of them was operated on by means of an "open" method with the aid of a pump-oxygenator, followed by some improvement, and in the other a "closed" method was used, with excellent result.

These 2 congenital anomalies of the mitral valve seem to be rare, and their prognosis is unfavorable. It is suggested that this diagnosis be more seriously entertained in the future and that surgical intervention be undertaken in these seriously ill children.

Simplified Technique for Direct Vision Pulmonary Valvotomy. C. R. Lam and R. E. Taber. J. Thoracic Surg. 38:309-318 (Sept.) 1959 [St. Louis].

If the surgeon is to make the best possible correction of pulmonic valve stenosis, he must be able to see what he is doing. This principle has been reluctantly accepted, because the transventricular method popularized about 10 years ago by Brock had many attractive features, and its immediate clinical results appeared to be satisfactory. A recent survey revealed, however, that many patients having been treated by the transventricular method required a second valvotomy by an open technique. The authors at first used open valvotomy with hypothermia, but observations on a woman who had a combination of atrial septal defect with pulmonic stenosis led them to carry out open pulmonary valvotomy without hypothermia. Since then they have used open pulmonary valvotomy without hypothermia and without the pump-oxygenator in 48 patients, with a single death which occurred in the youngest patient in the series, a child 18 months of age.

There have been no postoperative complications in the other 47 patients. In the short period of follow-up, clinical studies have indicated an excellent correction of the defect in every patient. In several cases the murmur has disappeared, and in all there has been a reduction in heart size and electrocardiographic evidence of less right ventricular hypertrophy. With the experience with the transventricular operation in mind, there may be skepticism about the long-term results. The operation is suitable only for pulmonic stenosis of the valvular type. Differentiation of this type from isolated infundibular stenosis and other congenital defects should be possible with the diagnostic techniques available.

The Etiology and Prevention of Atrial Fibrillation After Mitral Valvotomy. C. F. Kittle and J. E. Crockett. J. Thoracic Surg. 38:353-361 (Sept.) 1959 [St. Louis].

The authors reviewed the cases of 254 patients who had undergone mitral valvotomy at the University of Kansas Medical Center in Kansas City, Kan., and the Kansas City (Mo.) Veterans Administration Hospital since 1953, giving particular attention to the occurrence of postoperative atrial fibrillation and the prevention of this arrhythmia. Ninety-nine of the 254 patients had atrial fibrillation before the operation, and 155 had a normal sinus rhythm preoperatively. Atrial fibrillation developed after operation in 41 (26%) of the 155 patients, this being the commonest complication after mitral valvotomy. Atrial fibrillation usually developed between the 2nd and the 4th day after the operation, although it began as early as the 1st and as late as the 15th day. The occurrence of the fibrillation was not related to the age of the patients.

The frequency of postoperative atrial fibrillation was significantly lower in those patients receiving both digitalis and quinidine postoperatively. It is concluded that the combined use of these drugs is beneficial in preventing this deleterious arrhythmia. Local trauma to the left atrium incident to the atriotomy is probably the most important factor in the etiology of this arrhythmia. Conversion of postoperative atrial fibrillation to sinus rhythm can usually be accomplished, while this is more difficult in those with preoperative atrial fibrillation.

Congenital Hernia or Prolapse of the Diaphragm in Children. R. M. Konrad and A. R. Fahmy. Arch. klin. Chir. 291:253-270 (no. 3) 1959 (In German) [Berlin].

The authors feel that unfamiliarity with the symptoms and incorrect or belated diagnosis of congenital diaphragmatic defects are the chief reasons why newborn infants with such defects do not receive suitable surgical treatment, although improvements in anesthesia, in surgical techniques, and in preoperative and postoperative care during the past 2 decades justify immediate or early operation in such congenital thoracic dystopias of the abdominal organs. A knowledge of the ontogenesis of the diaphragm is essential for an understanding of the variety of its congenital defects. There are 2 main groups of organ dystopias in the chest during childhood. If the displaced abdominal organs are surrounded by a hernial sac, the dystopia is designated as a diaphragmatic hernia; in the absence of a hernial sac, the condition is referred to as a prolapse through the diaphragm. This differentiation is important not only from the anatomic but also from the clinical viewpoint.

The authors feel that all infants with congenital diaphragmatic hernia or prolapse, with the exception of those with hiatus hernia of the sliding type, who have symptoms during the first hours, days, or weeks should be subjected to surgical treatment, because such treatment is highly successful in comparison with the high mortality that results from conservative treatment. At present, in Germany, from two-thirds to three-fourths of the children with congenital deformities of the diaphragm still die within the first month of life. In some cases a correct diagnosis is never made, but the condition is designated as "dextrocardia"; in other cases valuable time is wasted with attempts at conservative treatment. The possibility of diaphragmatic defects should be taken into consideration in all infants who present with cyanosis and dyspnea.

The authors review data on 24 children with congenital diaphragmatic hernia or prolapse, who were observed at the surgical clinic in Düsseldorf during the past 8 years. All but one of these were subjected to surgical treatment. These children ranged in age from 1 day to 13 years. Of the 4 children who died (17% surgical mortality), 2 died within 4 hours. In these 2 children death was due to respiratory insufficiency, which, in turn, was caused by pulmonary hypoplasia; in one damage to the brain, caused by anoxemia during the preoperative phase, may have contributed to the fatal outcome. The third child died one month after operation of pneumonia, and the fourth 6 weeks after operation from an acute relapse. The 9 children subjected to follow-up examination were free from relapse.

Adenomatous Polyposis of the Stomach: Clinical and Anatomic Analysis of 20 Cases. G. Naldini and A. Salvini. Arch. ital. chir. 85:303-319 (no. 4) 1959 (In Italian) [Bologna, Italy].

The authors report on 20 patients with adenomatous polyposis of the stomach, who were operated on at the Institute for Pathological Surgery of the University of Milan, during the period from 1948 to 1957; 334 patients with malignant gastric tumor were operated on at the same institute during the same period. The 20 patients were 50 to 73 years of age; 11 were female, and 9 male. A family history of polyposis was present in 3 instances. Concomitant diseases were: hypochromic anemia in 15 patients, thyroid trauma in 2, uterine fibromatosis in 2, cholecystic calculi in 2, chronic colitis in 2, and lithiasis of the kidney in 1. The antrum and the corpus of the stomach constituted the most frequent localization in 11 patients. Nine patients presented diffuse gastritis – hypertrophic in 5, athrophic in 2, and mixed in the others. Seven patients presented simple polyps, and 4 atypical polyps; 13 (65%) of the 20 patients, therefore, presented either incipient or actual malignancy. In half of the patients the polyposis was diagnosed after the patient had suffered from dyspeptic disturbances for a period of 1 to 12 years. The disturbances were always related to meals. Five patients presented early postprandial vomiting, which was followed by relief of symptoms. Malignancy was found histologically in 3 of 9 patients who on roentgenologic examination had been diagnosed as carriers of benign tumors. A typical adenoma was found histologically in each of 5 patients in whom malignancy had been suspected on roentgenography. Two simple adenomas, 1 adenoma with incipient atypia, and 3 adenomas with malignant degeneration were found histologically in the other 6 patients who on roentgenologic examination had been diagnosed as having malignant gastric neoplasia. Fourteen patients were treated by subtotal gastric resections, and 6 by polypectomy. A normal postoperative course was observed in all the patients, with the exception of one who had been subjected to gastric resection. On follow-up examination 1 to 10 years after the operation, 8 patients were found in good general condition. One patient suffered from a local relapse due to adenoma 13 months after the operation. A peritoneal carcinosis appeared 3 months after the gastric resection in a patient in whom histological examination had shown a polyp with malignant degeneration. Two patients died of unknown cause, and 8 were lost to follow-up.

The authors point out that the difficulty of an exact clinical, roentgenologic, and even operative evaluation may be overcome by means of a rapid diagnosis with frozen sections made during the course of the operation. Because of the high incidence of incipient malignancy and of forms with a highly suspicious course, the authors suggest a radical operation whenever there are no contraindications. The good results obtained with polypectomy, however, show that even this type of operation may be beneficial if it is combined with an extensive excision of the gastric mucosa around the base where the tumor is implanted.

Symptomatology and Pathophysiology of Isolated Congenital Pulmonary Stenosis. A. Tsakiris, F. Schaub and A. Bühlmann. Schweiz. med. Wchnschr. 89:801-810 (Aug. 1) 1959 (In German) [Basel, Switzerland].

The authors report the clinical, electrocardiographic, radiologic, and hemodynamic findings in 11 male and 7 female patients, between the ages of 10 and 54 years, with isolated congenital pulmonary stenosis. Of the 18 patients, 6 had mild pulmonary stenosis, and 11 had moderate to severe pulmonary stenosis. The main symptoms of the 11 patients included reduced work capacity with exertional dyspnea, precordial pain at rest and during exertion, and tachycardia, but cyanosis was absent. The 6 patients with mild degrees of stenosis were usually asymptomatic and, in general, were able to lead a normal life without any complaints. On auscultation, the most prominent physical finding was a loud systolic murmur over the pulmonic area; it showed a "diamond shape" on the phonocardiogram and was frequently associated with splitting of the diminished second heart sound. The degree of splitting, i. e., the distance between the 2 segments of the second heart sound, is a reliable index of the severity of the stenosis. Five patients had, in addition, an atrial sound, and 7 had a systolic click. The chest roentgenograms of all 18 patients showed a prominent conus pulmonalis as a result of the poststenotic dilatation of the pulmonary arteries. Fourteen patients showed radiologic evidence of right ventricular hypertrophy. The right atrium was prominent in 13 patients, and a diminished pulmonary circulation was revealed by the chest roentgenograms of 9 patients.

The electrocardiograms of the 11 patients with more severe stenosis revealed a pronounced pattern of right ventricular hypertrophy and, in addition, impairment of the right side of the heart and an overload placed on the right atrium. Atrioventricular block was observed only once, and a right bundle-branch block twice. The pattern of right ventricular hypertrophy is of unique diagnostic significance, because it virtually never occurs in any other noncyanotic congenital heart disease. During cardiac catheterization the pressure gradient between the right ventricle and the pulmonary artery was always above 5 mm. Hg. The lowest right ventricular pressure was 35 mm. Hg, and the highest was 230 mm. Hg. The continuous recording of the pressure curve, as the catheter is drawn back from the pulmonary artery into the right ventricle, is of invaluable diagnostic aid in differentiating valvular from infundibular stenosis; of the 18 patients, 14 had valvular stenosis, 3 had infundibular stenosis, and in 1 patient the site of constriction could not be determined.

The surgical treatment of severe, isolated pulmonary stenosis was inaugurated by Brock and has become a generally recognized and routinely practiced procedure. Today the dilatation of the valvular opening or the resection in case of infundibular stenosis is being performed under direct vision on the open heart with the aid of hypothermia or a heart-lung apparatus and extracorporeal circulation respectively. The operative mortality rate, which first was relatively high for pulmonary valvulotomy and for the technically more difficult resection in case of infundibular stenosis, has been reduced from 20% to about 5% in favorable cases. The results concerning subjective complaints and general work capacity, as well as with regard to the reduction of pressure values in the right ventricle, appeared to be excellent. Patients with mild stenosis, whose work capacity has not been impaired, do not require treatment but should be carefully watched. The indications for operations should always be considered carefully in those patients who have considerable difficulties and an increased pressure in the right ventricle (limiting value: 80 to 100 mm. Hg).

The Surgical Treatment of Isolated Infundibular Stenosis. H. Swan, W. P. Hederman, P. S. Vigoda and S. G. Blount Jr. J. Thoracic Surg. 38:319-335 (Sept.) 1959 [St. Louis].

Subvalvular pulmonic stenosis with intact ventricular septum is more commonly referred to as "isolated infundibular stenosis." After citing previously published estimates on the incidence of this congenital cardiac defect, the authors present the histories of 5 patients with isolated infundibular stenosis, who were subjected to surgical treatment. Their ages ranged from 9 to 21 years. It appears that infundibular stenosis is caused by arrest of the normal involution of the bulbus cordis, which should be incorporated into the right ventricle by the end of the second month of intrauterine life, thus forming the outflow tract of the right ventricle. The stenosis may be of 2 types: 1. Fibrous and muscular tissues create a narrow area in some portion of the infundibulum, dividing the right ventricle into 2 chambers of unequal size, one with a hypertrophied wall, and the other dilated and thin-walled. 2. The infundibulum is shrunken in size, with thick muscular walls constituting a fusiform stenotic outlet. The authors did not encounter this second type in the 5 patients presented.

The symptoms, if any, of isolated infundibular stenosis are identical with those of valvular pulmonic stenosis and include exertional dyspnea, fatigue, syncope, dizziness, anginal pain, and, eventually, edema and right heart failure. Clubbing and cyanosis indicate the presence of a septal defect in both groups and rule out an isolated obstruction. The following points may help to differentiate infundibular stenosis from valvular stenosis: 1. Right ventricular precordial lift may be absent in very low infundibular stenosis. 2. The thrill and systolic murmur are usually maximal in the third left intercostal space in infundibular stenosis and higher up in valvular stenosis. 3. The second heart sound may be widely split in infundibular stenosis with a normal or diminished pulmonary component. 4. Usually no poststenotic dilatation of the pulmonary artery is seen on x-ray in infundibular stenosis and, in the right anterior oblique view, the left lower midsegment may bulge. 5. On fluoroscopy, the pulsations of the main pulmonary artery are increased in valvular stenosis, but not in the infundibular type. The only one of the above features which occurred constantly in the 5 patients presented was the lower site of the murmur and thrill; these were always louder in the third than in the first space. Right ventricular hypertrophy was present in both types of obstruction. A correct diagnosis of isolated infundibular stenosis was made preoperatively in 4 of the 5 patients.

Operation was performed under hypothermia, and the obstructing tissue was resected under direct vision via a ventriculotomy. It was found that hypothermia was suited ideally for the surgical treatment of isolated infundibular stenosis, since either valvular or infundibular obstruction can be effectively and safely treated with this technique alone. As a result of the treatment, 2 of the 5 patients had mild residual gradients, 1 had no gradient but a mild pulmonary hypertension (50 mm. Hg), while the other 2 had normal hemodynamics. All the patients were much improved clinically, and it is felt that they now have cardiovascular physiology compatible with full exercise and long life. Since this report was made, 3 additional patients have been operated on by the same method with excellent results.

Clinicopathologic Correlation in Thromboembolism. W. W. Coon and F. A. Coller. Surg. Gynec. & Obst. 109:259-269 (Sept.) 1959 [Chicago].

The authors attempted to demonstrate some of the vagaries and difficulties in the diagnosis of thromboembolic disease by reviewing the autopsies of 606 patients who had died of pulmonary arterial embolism at the University Hospital, Ann Arbor, Mich., between 1945 and 1954. The clinical records of the 606 patients were assessed with regard to the severity of associated disease and the prognosis on the basis of this disease; in addition, the nature of the terminal episode and the size, number, and location of emboli were considered.

The pulmonary embolism was thought to be the sole immediate cause of death in 198 patients, a contributory factor in producing death in 190, and of minor significance in 218. In only 7.1% of the 595 patients with autopsy-proved pulmonary emboli (excluding 11 on whom medicolegal autopsies were performed) had a definite clinical diagnosis been made prior to death. The correct clinical diagnosis of venous thrombosis was made even less frequently. Of 73 patients in whom venous thrombi were found in the iliac veins or the inferior vena cava, only 37 presented clinical manifestations of deep venous thrombosis. There was no demonstrable edema or other clinical sign in the remaining 36 patients despite the fact that iliac venous occlusion was present. The authors found that there are no specific diagnostic signs in pulmonary embolism. Chest pain and hemoptysis are infrequent and, when they are present, usually reflect the presence of pulmonary infarction. The differentiation of phlebothrombosis and thrombophlebitis on the basis of embolic potential is not only fallacious but dangerous.

Some pulmonary emboli in this series had no effect with regard to the patient's ultimate survival, either because they were minor emboli or because major emboli occurred in a patient who would have died even had the embolism not occurred. Even eliminating this group, death in 6% of the entire autopsy population might have been forestalled had pulmonary embolism not been present; in a third of this group there was little question that pulmonary embolism, which should be considered as a wholly preventable disease, was the sole cause of death. The clinician must assume much greater clinical awareness of the frequency of thromboembolism and be willing to make a presumptive diagnosis and treat with anticoagulants on the basis of suspicion alone. It is only in this way that one can hope to achieve anything by this approach in the salvage of more patients from fatal pulmonary embolism.

Splenic Pulp Manometry as an Emergency Test in the Differential Diagnosis of Acute Upper Gastrointestinal Bleeding. W. F. Panke, L. M. Rousselot and A. H. Moreno. Surg. Gynec. & Obst. 109:270-278 (Sept.) 1959 [Chicago].

In an attempt to differentiate esophagogastric varices from other sites of upper gastrointestinal hemorrhage during the acute bleeding episode, the authors used emergency percutaneous splenic pulp manometry in 113 patients who had recently bled or were actively bleeding from the upper gastrointestinal tract. Thirty-three of the 113 manometric readings were obtained as the initial discriminatory test during an acute bleeding episode. The remaining 80 readings were recorded some time after bleeding had ceased. Diagnosis of portal hypertension and varices was further substantiated by portography. Pressures were determined by inserting a no. 18 gauge spinal needle into the spleen. Local anesthesia was routinely used in the adult patients. The needle was inserted 1 to 3 cm. into the splenic pulp, depending on the degree of enlargement of the spleen. A constant drip of blood from the needle usually confirmed the intrasplenic location of its point. The needle was subsequently attached to a water manometer with its zero point at table level. A short length of rubber or plastic tubing interposed between the needle and the manometer prevented a rigid system and minimized the possibility of laceration of the spleen during subsequent respiratory motions. The average of 3 sequential readings was adopted as representative of the splenic pulp pressure. The corrected baseline for transposition to portal pressure was taken at 12 cm. above the plane of the table on which the patient was lying supine.

Data obtained subsequently to manometry established esophagogastric varices as the site of bleeding in 66 patients. The remaining 47 patients bled from other lesions. Splenic pulp pressures of patients who had bled from varices were consistently higher than those of patients who had bled from other causes. The mean pressure of patients bleeding from varices was 413 mm. of water. The mean pressure of patients bleeding from other sites in the upper gastrointestinal tract was 175 mm. of water. All patients whose pressures were above 290 mm. of water had bled or were bleeding from varices. If the pressure was below 250 mm., bleeding in all instances resulted from a lesion other than varices. There remained a narrow and delimited nondiagnostic area of overlap ranging from 250 to 290 mm. of water, which included patients bleeding from esophagogastric varices as well as patients bleeding from other lesions. Eleven patients, 4 bleeding from varices and 7 bleeding from other sites, had splenic pulp pressures in this area of overlap. In these patients, the findings of serial splenoportography were ultimately essential in determining the presence or absence of varices. Sixty-two (94%) of the 66 patients who bled from varices had pressures in excess of 290 mm. of water, and often in the range of 400 to 650 mm. of water.

Excellent correlation between portal tension and the degree of portal collateralization, as revealed by portography, had previously been shown. Splenic pulp pressure has proved to be a good index of actual portal vein pressure. The results obtained with splenic pulp manometry in the 113 patients showed that this method alone may yield valuable diagnostic information as to the presence or absence of varices. The procedure has proved to be 90% accurate. It is relatively simple, direct, practical, and safe. The immediate knowledge of the presence or absence of varices gained from its use has resulted in a more accurate appraisal and a more effective management of these patients.

Late Results in 110 Patients with Abdominal Aortic Aneurysm Treated by Resectional Placement of Aortic Homograft. L. O. Sheranian, J. E. Edwards and J. W. Kirklin. Surg. Gynec. & Obst. 109:309-314 (Sept.) 1959 [Chicago].

The authors report on 110 patients with aneurysms of the abdominal aorta, who were operated on at the Mayo Clinic between 1953 and 1957. The aneurysms were resected, and an aortic homograft was used to replace the excised vessel. One hundred four of the 110 patients had elective operations for nonruptured aneurysms, and 6 had emergency operations for ruptured aneurysms. Of the 104 patients without rupture of the aneurysm, 15 (14.4%) died in the hospital; of the 6 patients with ruptured aneurysm, 3 (50%) died in the hospital. In 8 (44%) of the 18 hospital deaths, postoperative hemorrhage related to homografting was the cause. In 5 of these, the hemorrhage was due to rupture of the homograft wall, and in 3 the hemorrhage seemed to originate at suture lines. Of the 92 patients who left the hospital after resection of the aneurysm and insertion of the homograft, 8 died in the course of the following 4 years. Failure of the homograft accounted for 3 of these deaths, occurring 2½, 1½, and 1½ years after the operation. Altogether, failures related to the use of homografts accounted for 11 (42%) of the total 26 hospital and late deaths. These 11 deaths occurred among 10% of the entire group of 110 patients treated by resection and homograft.

Of the patients surviving the operation and traced for 3 years, 84.8% were found to be living. This compares favorably with the expected 3-year survival rate of 89.5% for the normal population group at the average age of 63 years, which was the average age of the patients at operation. The survival rate of the patients with aneurysms of the abdominal aorta treated by resection and grafting was better than that in Estes' series of 102 patients with untreated aneurysms of the abdominal aorta. Homografts in the abdominal aorta, however, are not without serious specific complications, primarily rupture of the wall of the graft, which has occurred both early and late in the postoperative period. Plastic prostheses may prove advantageous in avoiding the problem of graft failure observed when homografts are used.

Valvotomy as a Curative Operation for Simple Pulmonary Stenosis. M. Campbell. Brit. Heart J. 21:415-428 (July) 1959 [London].

Campbell considers "simple pulmonary stenosis" the best term for pulmonary valvular stenosis with a closed ventricular septum, whether the foramen ovale is unsealed, in which case central cyanosis will develop if the stenosis is severe enough, or whether it is sealed, in which case there cannot be central cyanosis, however high the right ventricular pressure. He points out that 4 years ago he, together with Brock, reported the results of pulmonary valvotomy in 58 patients with this defect. They gave the following reasons for considering this a good operation: It relieved the symptoms and cyanosis, if these were present; in addition, it enabled a large heart to become smaller and reduced the strain on the right ventricle. Campbell now reports the further progress of these 58 patients and of another 18 operated on up to the end of 1956, making 76 in all. There were 13 more acyanotic and only 5 more cyanotic patients, making a total of 46 acyanotic and 30 cyanotic. The main purpose of this study was to assess the results more critically and to consider how far pulmonary valvotomy for simple stenosis can be considered a curative operation. More patients have been recatheterized, and the significance of the pressure reading taken at operation is now better understood. For patients who had not reached the stage of congestive heart failure, the operative mortality was under 6%. Only one patient failed to obtain any benefit, and this was because his stenosis was not recognized as infundibular.

This report is concerned chiefly with 57 patients, the others having been disregarded mostly because they were lost to follow-up. Thirty-five (61%) of the 57 patients, including similar proportions of acyanotic and cyanotic patients, improved enough to be able to lead normal lives, and none has lost any of the improvement that was gained. Another 22 patients (39%) were improved, often greatly, but they still had significant pulmonary stenosis that may prove harmful in the future. Most of the patients with the best results were under 16 years of age, and only 4 were over 20; on the other hand, nearly half of those who were only improved were over 20. One reason may be that good reduction of the gradient is more difficult because the valve and the outflow tract have become more rigid, but it is thought that sometimes it is because the fibrosis of the right ventricle has become irreversible. Therefore, patients should be operated on at an earlier age, as soon as convenient and always before they are 17. After 25 anything approaching a curative operation becomes much less likely.

The impression was gained that valvotomy should be performed on patients with less severe stenosis than existed in those operated on in the past. At first with so many patients waiting, most of those operated on had right ventricular systolic pressures of 100 mm. Hg, but Campbell now thinks that a systolic gradient of 50 mm. across the pulmonary valve indicates the need for valvotomy. Patients with an average residual gradient of less than 30 mm. have done very well, but those with one of over 50 mm. leave much to be desired. Gradients of 25 to 30 mm. are not of much importance, whether they are natural, as in cases of very slight stenosis, or residual, after surgical relief of a larger gradient. The great importance of continuing long-term studies for many years is emphasized, since there is no other way of obtaining the information that is necessary for giving the right advice to patients.

PATHOLOGY

Teratoma of the Lung. F. C. Collier, E. A. Dowling, D. Plott and H. Schneider. A. M. A. Arch. Path. 68:138-142 (Aug.) 1959 [Chicago].

The authors report a case of benign teratoma arising in the upper lobe of the left lung in a 46-year-old woman who was admitted to the University Hospital in Birmingham, Ala., in April, 1958. Eleven cases from the literature are also reviewed. Benign teratomata are mostly of the "dermoid cyst" type, i. e., consisting largely of ectodermal derivatives. The similarities of structure and symptomatology make it most likely that teratomata of the lung and the mediastinum have a common genesis. The third pharyngeal pouch, which according to Schlumberger represents the anlage of the thymus, is suggested as the most reasonable explanation of the genesis of these teratomata. The third pharyngeal pouch is entodermal, being invested by mesenchyme but also being in close contact with the cervical sinus, which is part of the ectodermal third branchial cleft. Thus, tissues from any of the 3 fundamental germ layers may be represented in these teratomata. In support of this thesis, it is pointed out that teratomata of the mediastinum always occur in the vicinity of the thymus and frequently are in intimate contact with this gland.

New Morphologic Aspects of Pulmonary Aspergillomas: Probable Initial and Residual States. J. C. Pimentel. Gaz. méd. port. 12:333-348 (March-April) 1959 (In Portuguese) [Lisbon].

From a study of 205 specimens removed during surgical operations for various pulmonary conditions, 15 cases of aspergilloma were detected. In 4 cases the pathological changes characteristic of the pulmonary aspergilloma were not translated into radiologic or clinical signs. The macroscopic examination of the specimens revealed cavities of an irregular ovoid shape, apparently epithelized, filled with a yellowish gray mass, the size of a pine cone. The cavities were lined with a layer of a similar structure, thicker at some points, creating the impression of protuberances. The pulmonary parenchyma outside the cavities presented numerous ectatic bronchi and small caseous encapsulated foci. The microscopic examination revealed a wall rich in fibrous tissue, covered with a simple cylindrical epithelium and, in small areas, with metaplastic epithelium. In one case the fungous culture permitted the identification of Aspergillus fumigatus; in the other 3 cases the sections, already fixed in Formalin, did not yield any culture. The mycelian masses presented 2 different morphologic aspects which were interpreted as the histological aspects of live and dead fungi respectively. In 3 cases both aspects were observed, while in one there was only the aspect of a live fungus.

In the other 11 specimens, classified as pathological structures of residual aspergilloma, the 2 characteristic features were a picture of infected bronchiectasis and the presence of a necrosed and softened mycelian mass in the lumen and in the granulated tissue of the ectatic bronchi. The mycelian mass had the aspect of dead fungi, and was approximately the size of a grain of corn, localized in the interior of a tuberculous cavity in full activity.

The findings are interpreted as indicating that in the pathological structure of pulmonary aspergilloma the fungus is not exactly a pathogenic agent. The process is fundamentally identical with that caused by the presence of an endobronchial foreign body. It seems that an overt antagonism exists between the fungal proliferation and a serious bronchopulmonary infection, leading to the regression of the mycelian mass. In this situation the diagnosis can only be made through a detailed microscopic study of the endocavitary mycelian mass and of the cavitary wall.

The Diagnosis of Intra-atrial Tumors and Tumorlike Formations. V. A. Zhmur. Klin. med. 37:27-34 (July) 1959 (In Russian) [Moscow].

The article analyzes observations on 6 patients with various cardiac diseases in whom autopsy demonstrated tumors of the atria. Literature data, as well as the author's observations, show that the tumors are usually myxomas, localized in the left atrium of the heart. Clinically, this disease resembles most frequently the clinical picture of mitral stenosis. Developing tumors of the atrium manifest the following syndromes: (a) obliteration of the atrial cavity; (b) occlusion of the atrioventricular orifice; and (c) embolism of vessels. On the basis of studies of the literature and the observations described, the author considers diagnosis during life quite feasible. Diagnosis during the life of the patient should direct the surgeon's endeavor to the operative removal of this neoplasm.

Malignant Pleural Mesothelioma: A Case Report With Autopsy Findings. D. S. Kahn, A. Glay and P. Madore. J. Thoracic Surg. 38:225-234 (Aug.) 1959 [St. Louis].

The authors report a primary malignant tumor of the parietal pleura in a 43-year-old man admitted to St. Mary's Hospital in Montreal in September, 1955. A thoracotomy with removal of the main tumor was performed, but diaphragmatic pleural implants precluded complete removal. The patient died one year after the operation. At autopsy, a second tumor showed a predominantly sarcomatous pattern with only rare foci of epithelium-like structure, usually in relation to free surfaces. There was widespread involvement of adjacent structures, evidence of spread through the diaphragm, and one microscopic metastatic focus in an adrenal. However, the specimen removed at operation had shown an epithelium-like structure with cells arranged in tubular and papillary fashion. There were no fibroblastic or sarcomatous features.

The controversy concerning the origin of pleural tumors centers around the necessity of explaining the 2 types of tissue, epithelial and fibrous, sometimes found in these tumors. As the tumor removed at operation had almost no fibroblastic component, consisting of cells resembling epithelial cells, and the tumor at autopsy had in the main a sarcomatous pattern with only a few epithelium-like areas, it is felt that the case reported demonstrates clearly that the epithelium-like and sarcomatous components found in primary tumors of the serosal cavities represent morphologic variations of the same neoplasm. There does not appear to be enough evidence to decide unequivocally whether these are truly primary tumors of a specialized structure, the mesothelium, with an embryonic potential to produce both epithelial and fibrous tissue elements, or whether they are fundamentally fibrous tissue tumors in which cells with an altered form, resembling epithelial cells, may be found.

Malignant synoviomas, which histologically closely resemble these pleural tumors, are accepted as fundamentally sarcomatous. The term "mesothelioma" is then probably not fully justified from an academic point of view. From a practical point of view, however, it serves a purpose in denoting a tumor arising primarily in the serosal cavities, which has a varied histological structure and which, when malignant, has a rather uniform growth pattern with extensive invasion but with little tendency to metastasize.

Observations on a Patient with the Malignant Carcinoid Syndrome. J. A. Kirkland, R. Cass, K. G. Lowe and S. F. Soutar. J. Clin. Path. 12:362-371 (July) 1959 [London].

The 62-year-old woman, whose history is presented, had had vague upper abdominal pain for about a year, and had lost weight for about 6 months. On examination, a mass was found in the right side of the hypochondrium. At laparotomy a Meckel's diverticulum, containing a hard nodule, was removed, and one of many metastatic deposits in the liver was taken for biopsy. Examination of the nodule in the diverticulm revealed that it was an argentaffin carcinoma (carcinoid tumor) which showed an unusual glandular structure. The specimen taken from the liver for biopsy revealed almost complete replacement of liver parenchyma by argentaffin carcinoma, with the same glandiform structure as was seen in the nodule in the diverticulum. The patient enjoyed reasonable health for some months, but the liver continued to enlarge and the patient needed increasing amounts of codeine for relief of pain. She died about 10 months after the operation.

During the last 9 months of the patient's life studies were made on the 5-hydroxytryptamine (5-HT) (serotonin) in her blood, and on the 5-hydroxyindolacetic acid (5-HIAA) in the urine. After death various body tissues were subjected to chemical analysis. The figures for 5-HT and for 5-HIAA obtained in this patient indicated that she had a functioning malignant carcinoid syndrome. At autopsy the 5-HT content in a lymph node metastasis was 2 mg. per gram of tissue, that is, it was comparable to the findings in other cases of malignant carcinoid syndrome.

Special attention was paid to the staining properties of the tumor cells because of the suggestion by others that there are argentaffin and argyrophil types of tumor cells. It has also been suggested that argentaffin cells secrete 5-hydroxytryptamine (5-HT) and argyrophil cells secrete 5-hydroxytryptophan (5-HTP). Comparison of various staining methods (including the silver methods) and the various fixatives used, with particular note of the cytological quality of the sections, led the authors to conclude that the new method of Lendrum and Fraser is more informative. Studies on the tumor cells suggested that there is only one type of neoplastic cell. In the lung and in the arterioles, histological changes were observed that may be a clue to the pulmonary hypertension of the carcinoid syndrome. It is suggested that the circulating 5-HT might act on the elastica of the pulmonary vessels and thus be the first link in the chain of causation of the pulmonary hypertension.

Latex-Fixation Test in Rheumatoid Arthritis: I. Clinical Significance of a Thermolabile Inhibitor. A. F. Schubart, A. S. Cohen and E. Calkins. New England J. Med. 261:363-368 (Aug. 20) 1959 [Boston].

The authors studied the serums obtained from 418 patients with articular disease seen at the arthritis clinic of the Massachusetts General Hospital, Boston, and from 360 patients seen at the medical clinic of this hospital, with the aid of the latex-fixation test (F-II L. P. test), both before and after heat inactivation at 56 C (132.8F) for 30 minutes. The results showed a striking difference between the native and inactivated serums. In many, a prozone inhibition was present, usually in dilutions of between 1 to 10 and 1 to 640. In the serums of 25 of 177 patients with definite rheumatoid arthritis, i. e., in significant numbers, total inhibition was present in the native serum, whereas, after heat inactivation, a positive reaction of the serum to the test was found in titers as high as 1 to 5120. Total inhibition was also seen in serums of patients with rheumatoid spondylitis, lupus erythematosus disseminatus, chronic rheumatic heart disease, ochronosis, leprosy, nontoxic goiter, diabetes mellitus, and several other diseases.

The reported results indicate that the thermolabile inhibitor may be demonstrated in any serum that contains agglutinating activity in the F-II L. P. test. The advantage of heat inactivation of the serum seems to be predominantly that of eliminating an unstable factor from a serologic system and thus increasing the reproducibility of the tests, which become more sensitive with an apparent loss of specificity. The latex-fixation test was slightly modified in the authors' study by reduction of centrifugation speed to accentuate the inhibition phenomenon. An increase in the concentration of gamma globulins used resulted in reduction of inhibition. The decrease of gamma globulin concentration created a higher degree of inhibition. The frequency of positive F-II L. P. tests in various rheumatic diseases, as well as certain other disorders, stresses the nonspecific nature of the test. The relation between duration and activity of disease and titer in the F-II L. P. test has not yet been fully clarified. Pending further data on this point, it appears that detailed classification of patients, as well as standardization of the method of the test, is desirable to produce results that are comparable.

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The authors conclude that cancer is a disease due to chronic stress. The adrenals play a role in the evolution of cancer and of its metastases by stimulating hypersecretion of stress substances from the anterior part of the pituitary. In patients with cancer of the breast with metastases, the stress diminishes after adrenalectomy, thus resulting in great improvement of the acute symptoms.

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The authors report on 126 children and adults who received 220 courses of roentgen irradiation combined with the intravenous administration of actinomycin D, an antibiotic and carcinolytic agent, at the Children's Cancer Research Foundation of the Children's Medical Center in Boston. The following observations were made. Some neoplasms, such as the malignant melanoma, usually considered to be radioresistant, responded well to combined therapy in some patients. The most favorable responses were obtained in patients with nephroblastoma (Wilms's tumor), Ewing's sarcoma, hemangioendotheliosarcoma, and rhabdomyosarcoma, definite improvement resulting after about 75% of the courses of combined therapy given to these patients. Simultaneous chemotherapy and irradiation therapy in low doses appear to be as effective as higher doses of either modality in certain instances. There is some evidence for a longer lasting beneficial effect with combined therapy. There is no apparent "cross resistance" between the 2 forms of therapy, even though it would appear that there is some gross similarity between some of their methods of action. Neoplasms may develop a resistance to the combination of agents, after which they are also refractory to either one alone. Potentiation of roentgen irradiation effects on normal tissues did not limit the total amount of roentgenotherapy that could be given to any patient. Interruptions to allow recovery, however, were not infrequent. Striking effects were obtained in tumors without apparent enhanced reactions in the skin or mucous membranes.

These findings suggest that irradiation responses in normal tissues and certain malignant tumors are enhanced when roentgen irradiation is combined with intravenous administration of actinomycin D. Normal structures react after smaller doses of irradiation than are ordinarily required to produce a like effect, and the healing processes thereafter proceed at a more rapid rate. Actinomycin D alone can reactivate latent irradiation effects in tissues which have been previously irradiated but have returned to normal in appearance. The reaction grossly is identical in type and distribution to that produced by the roentgenotherapy given earlier.

Modification of Late Irradiation Injury with L-Triiodothyronine. A. S. Glicksman, R. W. Rawson and J. J. Nickson. Radiology 73:178-190 (Aug.) 1959 [Syracuse, N. Y.].

Some of the authors initially noted in patients with carcinoma of the thyroid, who had severe irradiation changes of the skin and subcutaneous tissues, that production of hyperthyroidism seemed to produce a beneficial effect on these postirradiation changes. In an attempt to explore the role of exogenous thyroid hormones in the management of established irradiation damage, 75 patients in the irradiation damage clinic of the Memorial Center for cancer and allied diseases in New York were treated with liothyronine (3,5,3′-L-triiodothyronine [T-3]), which was selected because of the rapidity of its action as well as the promptness with which it is excreted by the body. The patients were started on 25 mcg. of the drug, given twice daily, and this dose was gradually increased to 200 mcg. per day, according to clinical judgment. Some patients were carried on 200 mcg. per day for more than 2 years. Of the 75 patients, 46 had ulcerations of the skin and subcutaneous tissues 2 to 20 years after irradiation, 24 had late irradiation fibrosis, and 5 had pulmonary fibrosis. Of the 46 patients, 13 were lost to follow-up, and of the remaining 33 who received T-3 for periods long enough to warrant evaluation, 10 showed excellent improvement, 18 good improvement, and 4 fair improvement; the condition of one was made worse. Of the 24 patients with late irradiation fibrosis, 8 were lost to follow-up, and of the remaining 16, 4 showed an excellent response, 7 a good response, 2 a fair response, and 3 were therapeutic failures. Of the 5 patients with pulmonary fibrosis, 1 was lost to follow-up, 1 showed good response with return of maximum breathing capacity to preirradiation levels, 1 showed only fair response, and 2 were therapeutic failures. Of the patients with damage being present from 2 to 30 years, over 50% showed good to excellent response to T-3 therapy. This would indicate that late irradiation changes exist in a dynamic state and that it is possible to modify them by altering the metabolism of the damaged tissue.

Supervoltage (2-Mvp) Rotation Irradiation of Cancer of the Bladder. M. Friedman. Radiology 73:191-208 (Aug.) 1959 [Syracuse, N. Y.].

The author presents a preliminary report on 81 patients with cancer of the urinary bladder, who were treated with 2 million volt x-ray irradiation by the rotation technique in the radiation therapy department of the Hospital for Joint Diseases in New York between 1951 and 1958. The patients had been subjected previously to various types of surgical procedures, and most of them had extensive and advanced lesions. Twenty-one patients (25%) had primary tumors, and 60 (75%) had recurrent tumors. The patient stood erect on a rotating platform during supervoltage irradiation; the target axis distance was 125 cm., and the exposure dose rate at the axis of rotation was 57 rads (units of measurement of the absorbed dose of ionizing irradiation) per minute. In most patients the field size at the axis of rotation was 8 by 8 cm. Occasionally when an advanced cancer infiltrated the pelvis, the field size was enlarged to 12 or 15 cm. in horizontal diameter. Its vertical height was seldom higher than 10 cm. because of the danger of irradiation injury to the small intestine.

A 3-year survival rate of 22% and a 5-year survival rate of 13% were obtained with the supervoltage rotation irradiation technique in this group of patients. Doses of from 8,000 to 10,000 rads, given within 40 to 60 days, proved successful. An occasional patient required larger doses. These doses are higher than those reported by other workers. Their use was dictated by the findings at serial cystoscopic examination, followed by biopsy, during treatment, and by the frequent finding of residual disease after the administration of doses ranging from 7,000 to 8,000 rads. The author cannot yet reconcile his large doses with the smaller doses reported by other workers, but he believes that advanced highly malignant cancers of the bladder require large tumor doses. These large doses can be given only with a well-collimated beam of supervoltage x-rays or gamma rays, with a precision beam-aiming technique. In order to improve the results of irradiation of cancer of the bladder, the prevalent practice of multiple surgical procedures preceding the irradiation will have to be discontinued, and irradiation started when the disease is in an earlier phase. Radiation cystitis is more severe after supervoltage rotation irradiation than after irradiation performed with the central-source intracavitary technique. The irradiation results in the patients treated for primary tumors with a 3-year survival rate of 42% were better than in those treated for recurrent tumors with a 3-year survival rate of 18%.

The unusual case of a 35-year-old woman is described; this patient had a grade 3, large, fungating, infiltrating carcinoma on the left lateral wall of the bladder which was radioresistant. She was given a maximum tumor dose of 13,200 rads in 90 days, and the disease was controlled. Injury to the intestines was corrected surgically, and the patient is alive without evidence of cancer 6 months after the completion of the supervoltage rotation irradiation treatment. However, comparison of the results of the supervoltage rotation irradiation in this group of 81 patients with those in a group of 50 patients treated by the author with central-source intracavitary irradiation has suggested that the latter technique is superior to supervoltage rotation irradiation for cancer of the bladder, since it yielded a 5-year survival rate of 56% as compared with the 5-year survival rate of 13%.

Supervoltage Irradiation in Bladder Carcinoma: 1952-1958. P. Rubin and R. Buran. Radiology 73:209-225 (Aug.) 1959 [Syracuse, N. Y.].

The authors report on 51 male and 10 female patients with carcinoma of the bladder, most of them between the ages of 60 and 80 years, who were treated with one million volt x-ray irradiation by the rotation technique at the Strong Memorial Hospital in Rochester, N. Y., between 1952 and 1958. The commonest presenting symptoms were hematuria (57%), frequency (51%), and dysuria (38%). Nocturia occurred in 16%, and pain in 15%. On cystoscopic examination 38 (63%) of the 61 patients had multiple lesions as opposed to solitary papillary lesions. The most frequent anatomic sites of origin were the trigone (33%) and bladder neck (33%), followed by the lateral walls (21%) and diffuse involvement (16%). The fundus was involved in 5%, the posterior wall in 7%, and the anterior wall in 5%. The daily tumor dose generally was 200 r at the axis of rotation, and the total dose administered to these patients ranged from 5,000 to 6,000 r in 5 or 6 weeks, with doses of 3,000 to 4,000 r reserved for palliative rather than curative purposes. The field size usually ranged from 8 by 8 to 10 by 10 cm. If extensive pelvic disease was present, larger fields, up to 15 by 15 cm., were employed. Cystoscopy was performed at the end of the treatment, with repeat examinations scheduled every 2 to 4 months during the first year and at lengthening intervals as the disease appears to be controlled.

The results obtained in these patients warrant the following conclusions. The principles of treatment of tumors of the bladder are dependent on the classification of each patient according to primary and secondary considerations. For group 1, consisting of patients with superficial-stage, low-grade carcinoma, the initial treatment of choice is a conservative surgical measure, such as fulguration, transurethral resection of the tumor, or segmental resection. As the lesions recur, become multiple in origin, and change their histological grade and depth of invasion, more radical measures are justified. Supervoltage irradiation should be employed only as an alternative to total cystectomy and not as a prophylactic measure. Sixteen of the 61 patients were in this group; 6 patients were controlled by irradiation, and 5 survived without disease for periods ranging from 6 months to 4 years and 3 months. For group 2, consisting of patients with deep-stage, high-grade carcinoma, supervoltage irradiation in curative dosage levels has the most to offer those with deeply invasive and aggressive tumors. Results suggest that cure rates are at least comparable to, and perhaps better than, those obtained by radical surgical procedures, with less morbidity and mortality. There were 26 patients in this group; 10 of them were controlled by irradiation, and 5 survived without disease for periods ranging from 2.3 to 5 years.

In group 3, consisting of patients with metastatic-stage, high-grade carcinoma, supervoltage irradiation as a palliative procedure can control pain and hematuria and is more easily tolerated than orthovoltage therapy. A diversionary measure, as an ileal bladder and ureteral transplantation, may be equally or more palliative in many cases than moderate doses of irradiation. In selected patients an ileal bladder may enable one to deliver a curative dose of irradiation and perhaps sterilize the primary lesion. There were 19 patients in this group, 18 of whom died and 1 is alive with persistent carcinoma. Any modality of treatment, including supervoltage radiation therapy, failed. Last and of most importance are cooperation between the patient and the physicians responsible for treatment and follow-up and cooperation between the urologist and the radiologist, since in a large number of patients more than one modality of treatment will be used.

Percutaneous Splenoportography: Evaluation of Clinical Indications: Importance in the Study of Portal Hypertension. C. Larrain, C. Zuñiga, G. Labatut and others. Rev. méd. Chile. 87:410-420 (June) 1959 (In Spanish) [Santiago].

Percutaneous splenoportography was performed on 56 patients hospitalized in the Hospital Aguirre of Santiago, Chile. A percutaneous injection of an opaque substance was made into the spleen during a period of 9 seconds, roentgenograms being taken at the 3rd, the 6th, and the 9th second after the injection. Normal features of splenoportography were shown by an even opacification of the entire splenoportal system, including the fine intrahepatic portal branches, within 3 seconds after the injection. There were no splenoportal collaterals, and the lumens of both the splenic vein and the portal vein were normal. In portal hypertension the splenoportal system became opacified within 6 to 9 seconds after the injection, with faint showing of the fine intrahepatic portal branches. The splenoportal venous system was hypertensive, and there were engorged collaterals and varices.

Splenoportograms showed that, of the 56 patients, the splenoportal system became opacified in 51. Thirty-five of these patients had cirrhosis of the liver, and 28 had signs of portal hypertension in that they had had hemorrhages by mouth. Roentgenologic examination of the esophagus and endoscopy showed esophageal varices in 16 patients. Splenoportography showed a normal condition in 9 of the 35 patients with chronic cirrhosis of the liver, and in the remaining 26 it showed esophageal varices and splenoportal collaterals which had not been shown by roentgenologic examination of the esophagus or by endoscopy. Splenoportography was also of diagnostic value in patients with chronic myeloid leukemia, intrahepatic metastases of gastric carcinoma, and hydatid cysts of the liver. It followed a normal pattern of opacification in patients with liver abscesses, splenomegaly of uncertain origin, abdominal lymphosarcoma, alcoholic gastritis, and fatty liver. Percutaneous splenoportography is of value in the diagnosis of portal hypertension of either intrahepatic or extrahepatic origin. The procedure is harmless and is well tolerated by the patients.

Pulmonary Staphylococcia: Clinical, Radiologic, and Therapeutic Study. A. Roisinblit, L. Anunziato and W. E. García. Prensa méd. argent. 46:630-638 (March 13) 1959 (In Spanish) [Buenos Aires].

In the differential diagnosis of pulmonary staphylococcia, the radiologic aspects represent an important element, since the clinical picture is very similar to that of other lung diseases. The authors report 3 cases in which serial radiograms permitted the establishment of the diagnosis and the administration of adequate therapy. The radiologic signs are generally present from the 5th day after the onset of the disease, and they include pneumothorax, pneumatocele formation, variable infiltration with perifocal emphysema, early encapsulation of pleural effusion, and hilar enlargement.

The first patient, a 27-year-old woman, felt ill, with hypogastric pain, fever, and metrorrhagia, 24 hours after an induced abortion. As she subsequently developed dyspnea, oliguria, and jaundice, a radiologic examination showed signs of staphylococcic infection of the lungs, which was confirmed by the finding of Staphylococcus aureus in the sputum. The patient received Sigmamycin (a combination of oleandomycin and tetracycline) orally, then erythromycin. Although her condition improved, the same radiologic alterations persisted. As she refused surgical treatment, she was discharged from the hospital. Her condition deteriorated again, the clinical picture being that of septicemia, and the blood culture being positive for Staph. aureus. The intravenous administration of Sigmamycin brought temporary relief, but the patient died of blood dyscrasia. The second and third patients had similar radiologic signs of bilateral infiltration and cavitations. Antibiotic treatment (including Sigmamycin in one of the cases) resulted in recovery of both patients.

The authors insist on the necessity of taking into consideration the possibility of pulmonary staphylococcic infection in any case of acute lung disease. They consider the intravenous administration of Sigmamycin the most effective therapy available at present.

Aberrant Pancreatic Tissue in the Stomach. D. R. Rooney. Radiology 73:241-244 (Aug.) 1959 [Syracuse, N. Y.].

The author reports on 5 women and 2 men, between the ages of 32 and 71 years, with aberrant pancreatic tissue in the stomach. The commonest symptom usually ascribed to this condition is nonspecific epigastric pain; 6 of the 7 patients had this complaint. Pyloric obstruction is probably the next common symptom, and one of the patients had symptoms suggestive of partial intermittent obstruction with occasional attacks of distention. The roentgenologic findings in the 7 patients were strikingly similar. There was a solitary, sharply demarcated, round or oval filling defect, measuring 1 or 2 cm. in diameter and located for the most part in the gastric antrum within 6 cm. of the plyoric orifice. The distinguishing morphologic finding in aberrant pancreatic tissue in the stomach is a central duct structure which is not present in other intramural gastric tumors. When the radiologist finds a filling defect, such as the one described above, a careful search, aided by pressure spot-films, should be made for a central dimple in this nodule. This central pit or depression, when visualized, encourages the preoperative diagnosis of aberrant pancreatic tissue in the stomach, since this depression surrounds the orifice of the duct draining the aberrant pancreatic acini. This central duct was identified in the gross surgical specimens from each of the 7 patients. The visualization of this structure may be of great value to the radiologist and gastrocopist in the preoperative diagnosis, and to the surgeon or pathologist who may be confronted, in the operating room, with the decision of simple against radical gastric resection.

ANESTHESIA

Apnea Associated with the Intraperitoneal Use of Neomycin. C. H. Fredell and B. L. McElroy. Southwestern Med. 40:503-504 (Aug.) 1959 [El Paso, Texas].

The intraperitoneal instillation of neomycin has been of definite value in lowering the mortality rate due to peritonitis, but reports of apnea associated with the intraperitoneal use of neomycin have been published. Experimental work has been done to elucidate the etiology of this phenomenon. The action of neomycin seems to be a potentiation, or a combination, with the anesthetic agent, producing a neuromuscular blocking effect. The presence of peritoneal damage, however, allows more rapid absorption of the neomycin, consequently lowering the amount which might produce apnea. Experimental and clinical work has shown that the apnea can be treated effectively with neostigmine methylsulfate. Two cases are presented, demonstrating this unusual problem. The authors conclude that the dangers of the intraperitoneal instillation of neomycin during a general anesthesia, in the presence of peritoneal damage, far outweigh any benefits accrued by this practice.

The Combined Preparation Penicillin-Streptomycin-Procaine Hydrochloride in Local Anesthesia. C. Buccellato, A. Cittadini and F. Gargano. Minerva chir. 14:475-480 (May 15) 1959 (In Italian) [Turin, Italy].

The authors experimented, in vitro and in vivo, with the combined preparation penicillin-streptomycin-procaine hydrochloride for use as a local anesthetic in man. The experiments in vitro revealed that the combined antibiotic action of penicillin and streptomycin in a solution of either sodium chloride or procaine hydrochloride had a similar inhibitive action on the growth of a culture of staphylococcus pyogenes var. aureus. The experiments in vivo on 8 rabbits demonstrated that the combined preparation penicillin-streptomycin in a solution of either sodium chloride or procaine hydrochloride had the same degree of inhibitive action on the development of subcutaneous abscesses, which were induced by inoculation of a suspension of Staph. pyogenes var. aureus. The anesthetic action of procaine hydrochloride did not diminish because of its combination with the antibiotics.

The combination of penicillin, streptomycin, and procaine hydrochloride was then tested with patients under local anesthesia in 30 operations. No antibiotics were administered after the operation, and the operative wounds healed fast and in asepsis. The authors believe that the combined preparation penicillin-streptomycin-procaine hydrochloride has a twofold advantage: 1. A single administration of the preparation exerts simultaneously both anesthetic and antibiotic effects, which procedure saves time. 2. There is a more effective antibiotic action of penicillin and streptomycin if administered in combination with procaine hydrochloride.

PUBLIC HEALTH

Infectious Encephalitis in Colorado. L. E. Giddings, S. G. Copps and C. A. Sooter. Pub. Health Rep. 74:647-652 (July) 1959 [Washington, D. C.].

The authors report on the epidemiologic aspects of 258 cases of infectious encephalitis which occurred in Colorado between May, 1956, and December, 1957. Most of these cases occurred in the late summer and the early fall months of the 2 years. The ages of the patients ranged from 6 days to 82 years, but there was a marked preponderance of patients less than 20 years of age. As a rule, the cases of infectious encephalitis were roughly distributed in proportion to population density throughout Colorado. Serologic tests for various causative agents were performed. The causative agent was determined by laboratory or clinical means in 109 of the 258 cases. Arthropod-borne diseases, such as St. Louis encephalitis and western encephalitis, accounted for 73 of the 109 cases, while mumps accounted for 24 and miscellaneous agents for 12. The causative agent was unknown in 149 (57.8%) cases. There were 10 deaths among the 258 patients.

Comparison of the epidemiologic characteristics of the viruses of St. Louis encephalitis, western encephalitis, and mumps, which were the commonest causative agents, showed that the St. Louis encephalitis virus tends to infect persons of all ages, with a slight preference for the older age groups. The age distribution was somewhat alike for the western encephalitis and mumps viruses in that the diseases occurred primarily in persons aged less than 20 years. Mumps is a highly infectious disease, endemic in most areas of the country, which becomes epidemic whenever a sufficient number of persons who are not immune are present. As a result of the frequent epidemics, most persons become immune before reaching an advanced age. The incidence of St. Louis encephalitis and western encephalitis in a community is dependent on mosquito populations and mosquito infection rates and many other poorly understood factors. In the light of present-day knowledge, the age distribution differences between St. Louis encephalitis and western encephalitis cannot be explained. The preponderance of male patients infected with the St. Louis and western viruses could possibly be explained by the fact that men and boys, in general, spend more time out-of-doors and are, hence, at greater risk of exposure to infective mosquitoes. More diagnostic work needs to be done in the field of infectious encephalitis in order to evaluate the problem brought about by the large number of agents which can produce this syndrome.

Statistical Relevances on the Behavior of Brucellar Infection During the Period 1948-1957. A. Pane and G. Manzillo. Acta med. ital. 13:144-151 (June) 1958 (In Italian) [Rome].

Italy, according to a report of the World Medical Association, had 6,914 cases of brucellosis in 1955; it was the country with the highest frequency in an absolute sense, and it came after Argentina and Malta in relative frequency. The authors report on a statistical study of 467 patients with brucellosis who were observed from 1948 to 1957 at the "D. Cotugno" Hospital of Naples, where patients with this disease from both the city of Naples and the whole Campania region are treated. Brucellosis was most frequent in 1951 and 1953, 75 cases and 60 cases, respectively, being reported; it was least frequent in 1957, with 30 cases. An increase in the frequency of most infectious diseases was observed in 1953. Data for the years 1951-1957 showed that the highest monthly frequency occurred during April, May, June, and July, with 40, 46, 50, and 44 cases, respectively, which makes brucellosis a seasonal disease most frequent in the spring and summer. Two hundred ninety-four (62.95%) of the 467 patients were male, and 173 (37.05%) were female. Seventy-six patients were 15 to 20 years of age; 69 were 20 to 25; 61 were 11 to 15; 53 were 26 to 30; 26 were 6 to 10; 19 were 1 to 5; and 12 were 61 to 75. Data on brucellosis for the whole of Italy show that there has been a slight decline in the morbidity rate during the last few years.

British Standard Poliomyelitis Antisera Types 1, 2, and 3. F. T. Perkins and D. G. Evans. Brit. M. J. 1:1549-1553 (June 20) 1959 [London].

Standard antiserums to each of the 3 poliomyelitis virus types would make it possible to express the neutralizing potency of other serums in terms of the standard and allow a valid comparison to be made between the results obtained by different workers. In 1955 reference poliomyelitis antiserums were prepared to serve as controls in titrating poliomyelitis antibodies in both human and animal serums, but these antiserums were used essentially in insuring the consistency of the titration system and not in assaying serums in terms of units. For a number of reasons they were unsuitable for use as standards to which a unitage could be assigned. New freeze-dried preparations of antiserums to each of the 3 poliomyelitis virus types were, therefore, made.

A collaborative study, in which 5 laboratories took part, showed that close agreement was obtained among the different laboratories when the type 1, 2, or 3 neutralizing potencies of poliomyelitis antiserums were determined with reference to freeze-dried preparations of antiserums. It was, therefore, decided, with the agreement of those who participated in the study, to establish the 3 freeze-dried preparations of antiserums as British standard poliomyelitis antiserums, types 1, 2, and 3, and to assign to each a value of 10 units per ampul. It will now be possible to express the neutralizing potency of serums in terms of units and to abandon the unsatisfactory method of using titer-dilutions. The standard antiserums will be held by the department of biological standards, National Institute for Medical Research, Mill Hill, London.

The Question of Poliomyelitis Infection Among Hospital Personnel. P. Sachtleben and A. Schellenberger. Deutsche med. Wchnschr. 84:1142-1145 (June 19) 1959 (In German) [Stuttgart, Germany].

Every year a certain percentage of the population, particularly children, become infected with the virus of poliomyelitis, but the infection usually remains silent. Nevertheless, it is likely that a number of children in hospitals will excrete the virus, even though they show no active signs of poliomyelitis. This suggests that exposure is particularly great among the personnel of children's hospitals. In 1956 the authors made 3 determinations of complement-fixing antibodies against poliomyelitis on the venous blood samples of 65 persons on the staff of the Children's Clinic of the University of Munich. Physicians, nurses, and physical therapists were included. Forty-four children and 71 adults served as control groups. Physicians and senior nurses showed the same percentage of positive complement-fixation reactions (16%) as did the control group of adults, whereas among the young student nurses and the physical therapists in training the percentage was 50%. A diagram recording the seasonal incidence of positive poliomyelitis complement-fixation tests in the various groups shows an increase from summer to fall and a slight decrease from fall to winter. Discussing the cause of the differences between older and younger hospital personnel, the authors assume that the type of work performed, as well as the immunobiological processes, play a part. They assume that young adults contract chiefly first infections and heterologous reinfections, whereas in older persons (physicians and senior nurses) homologous reinfections are more frequent.

The Tetanus Problem in the South. A. N. Houston, W. A. Roy, R. A. Faust and D. M. Ewin. J. Louisiana M. Soc. 111:241-245 (July) 1959 [New Orleans].

Taking the figures available from 1952 through 1956, the death incidence of tetanus in the United States is 0.19 per 100,000 population. During these 5 years, 1,543 persons died of this disease in the United States, with an average of 309 deaths per year. The unequal geographical distribution of the incidence of tetanus, however, may be illustrated by selecting the 11 "Confederate States" as one area, and the 37 states remaining as a comparative area. The former contained 24% of the population of the United States but had 63% of the deaths from tetanus. This means 0.50 deaths per year per 100,000 population for the "Confederate States" compared with 0.09 for the other 37 states and 0.19 for the United States at large. Louisiana, fourth in the United States with regard to deaths per 100,000 population per year, led the nation for the single year 1956 with 0.72 deaths per 100,000 population. A campaign to warn and educate all in regard to the alarming prevalence of tetanus in Louisiana and the 11 "Confederate States" has been launched and emphasis has been laid on the need for protection against tetanus. A "suggested guide" has been put out by the committee on tetanus protection of the Orleans Parish Medical Society and the committee on trauma of the Louisiana chapter of the American College of Surgeons, concerning wound care and adequate basic and booster immunization with tetanus toxoid. Antitetanic serum (or tetanus antitoxin) does not attack the causative agent, Clostridium tetani, but merely neutralizes the toxin being produced by living organisms. This serum is most often of equine origin, and, because of the discomforts of the highly prevalent types of serum sickness or the dangers of anaphylaxis, it should not be given unless real indications exist. Antibiotics have no effect on the toxin already produced by living organisms; they attack only the organisms and do so best when given within a few hours of wounding and for some days thereafter.

The Incidence of Certain Endemic Enteric Virus Infections in Southern Louisiana. H. M. Gelfand. South. M. J. 52:819-827 (July) 1959 [Birmingham, Ala].

The author investigated the natural transmission of poliomyelitis viruses in 115 newborn children who were under the continuous observation of the epidemiology division of the Tulane University School of Medicine in New Orleans during the period from 1954 through 1956. Four hundred seventy-two serum specimens, obtained from members of the children's families or close associates, were collected and tested for their ability to neutralize prototype poliomyelitis virus strains. Findings showed a prevalence of neutralizing antibodies against poliomyelitis viruses, types 1 to 3, Coxsackie viruses, group A, type 9, and group B, types 1 to 5, and enteric cytopathogenic human orphan (ECHO) viruses, types 1 to 3, 5 to 12, and 14. Of the types investigated, only antibodies against ECHO viruses, types 4 and 13, were lacking in a final serum dilution of 1:10. There was a great variety in the age pattern of these several antibodies; some were similar to poliomyelitis virus, type 1, and others were markedly different. There appeared to be 4 general types of age-pattern curves, with several viruses represented by each. It has been suggested that these differences were more likely the result of variations among the types in the duration of detectable antibody than of variations in the ease of transmission within households.

Six hundred thirteen enterovirus strains were isolated from fecal specimens obtained from the 115 children. The poliomyelitis viruses, Coxsackie viruses, ECHO viruses, and adenoviruses were found most frequently, whereas some types were not isolated at all. The 3-year average of the percentages of children excreting viruses of all the isolated types by month shows a consistent seasonal variation, with maximal occurrence in summer and early autumn. There was a marked increase in transmission during the warmest months of the year. The interesting exception was ECHO virus, type 10, for which isolation was maximal during the winter months. No significant central nervous system or intestinal disease occurred coincidentally with these infections. The occurrence of an "epidemic" of ECHO virus, type 7, during 1956, which involved 34% of the children in this series, reemphasizes the caution that must be observed when these agents are isolated during an investigation of outbreak of disease.

BOOK REVIEWS

The Onset of Stuttering: Research Findings and Implications. By Wendell Johnson and associates. Cloth. $5. Pp. 243. University of Minnesota Press, Minneapolis 14; Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, England; Thomas Allen, Ltd., 266 King St., W., Toronto, Canada, 1959.

In approaching the problem of stuttering the author brings out the following two important points: first, that the label of stutterer is usually placed on a child by a lay person and, second, that many people other than those who are really informed on this problem presume to explain it and to suggest remedial procedures. The fact that a person is called a stutterer because someone thinks he is a stutterer suggests that the problem may sometimes be with the observer rather than with the child said to have the speech problem. The book contains complete reports on three extensive studies carried out at the University of Iowa under the direction of the author. A series of 500 children and their parents were included in the investigations, one half of the children having been classified as stutterers and the other half having been considered to have normal speech. The groups were carefully matched. With use of standard tests and complete as well as careful interviewing techniques, comparative data were gathered in reference to many factors which have been thought to be causative. The author states his purpose as being "to gather substantially more of the facts to be explained before yielding further to the manifestly human compulsion to make explanations."

The mass of data collected indicated that stutterers are really not different from nonstutterers but that their speech is initially perceived and evaluated differently, usually by a parent. The negative evaluations and misperceptions of the adults are communicated to the children, who then view their own speech in this same anxious and rejecting manner. The role of the listeners in fixing and intensifying nonfluencies in particular children, who are probably in reality having no more hesitations and repetitions than any other children learning oral language, has strong implications for all persons who are responsible for children, both professional and nonprofessional.

This book merits careful attention because the author has devoted much of his career to studying and thinking about the problem of stuttering. He has been the director of the speech clinic of the State University of Iowa where more research on stuttering has been produced over a longer period of time than at any other university. In a field in which there have been strong differences of opinion, it is satisfying to have an author present his rationale, his methods, and his data so completely. Misperceptions of stutterers by professional persons can place heavy burdens on the shoulders of children and their parents. Before "yielding further to *the manifestly human compulsion to make explanations*" it would be well for professional persons to read this book.

Physiology of Motion Demonstrated by Means of Electrical Stimulation and Clinical Observation and Applied to the Study of Paralysis and Deformities. By Dr. G. B. Duchenne. Translated and edited by Emanuel B. Kaplan, M.D., Attending Orthopedic Surgeon, Hospital for Joint Diseases, New York. Cloth. $11. Pp. 612, with 101 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

This translation makes some extremely interesting material available to readers who in the past may have been entirely unacquainted with the work of Duchenne or have had access only to translations of selected portions of his book. It is at once a compendium of detailed information and a mine of inspiration. Part 1, Motion of the Thoracic Extremity, is a fine analysis of the individual muscles of the hand, forearm, arm, and shoulder. Part 2, Movements of the Abdominal Extremity, deals similarly with the muscles of the foot and leg and those that move the thigh on the pelvis. Part 3 analyzes the action of the muscles that govern respiration and those that move the craniovertebral column.

The translator's introduction should be read for proper appreciation of Duchenne's originality. Duchenne worked on living subjects as well as cadavers, on animals as well as man, on the normal as well as the abnormal, and with electrical stimulation as well as voluntary movements. He showed how diverse are the movements obtainable from any given muscle when the position of the body is varied and how paradoxical the movements may seem when the muscle contracts in the absence of cooperation from its normal synergists and antagonists. The author's original illustrations are reproduced. They are somewhat primitive and not very numerous, but the text makes up for this lack by its vivid writing and the abundance of specific instances for every generalization. The translator has solved some difficult problems, especially that of rendering the anatomic names of muscles as written in French in 1867 into terms intelligible to readers of present-day English. The informed reader should

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recognize the phrase "muscular conscience" on page 561 as corresponding to the present term "proprioception" and will not likely be confused by the rendering of "disgraceful" on page 600, where the meaning intended was presumably "ungracious."

Medical students who are well along in the study of anatomy might do well to sample the pages of this book so as to gain an appreciation of the complexity of muscle action. The brief statements on this subject in most textbooks are necessarily simplified. To physicians and all others working in the field of physical medicine and rehabilitation, this book is highly recommended.

Synopsis of Ear, Nose, and Throat Diseases. By Robert E. Ryan, B.S., M.D., M.S. (ALR.), Associate Otolaryngologist, St. John's Hospital, St. Louis, William C. Thornell, A.B., B.M., M.D., Assistant Professor, Department of Otolaryngology, Cincinnati College of Medicine, Cincinnati, and Hans von Leden, M.D., F.A.C.S., F.I.C.S., Assistant Professor of Otolaryngology, Northwestern University Medical School, Chicago. Cloth. $6.75. Pp. 383, with 59 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton, 134 Great Portland St., London, W. 1, England, 1959.

This well-illustrated and finely printed volume, with its maroon color and black label with gold lettering, is pleasing to the eye, while the size permits it to be carried comfortably in the coat pocket. The book is well designed and well written and should fill the needs of the student, intern, resident, and general practitioner. Since most patients seen by the general practitioner each day present some disorder of the ear, nose, throat, or respiratory system, it is fitting that such a work should be available to him for guidance. In fact, this book could easily rank in value with the sister volume in ophthalmology by Dr. May. The material included agrees with the thinking of modern otolaryngologists and truly reflects the lengthening shadow of a great teacher, Dr. Henry L. Williams, of the Mayo Clinic. The three former fellows of the Mayo Clinic have dedicated this volume to their teacher and friend, and its composition is such that he might well be proud of it.

Das Röntgenschichtbild des Ohres. The Tomogram of the Ear. By Prof. Karl Mündnich and Dr. Kurt-Walter Frey. With introduction by Prof. Dr. A. Herrmann and Prof. Dr. H. v. Braunbehrens. Archiv und Atlas der normalen und pathologischen Anatomie in typischen Röntgenbildern. Band 83, Ergänzungsbände, Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin: Diagnostik, Physik, Biologie, Therapie. Herausgeber: R. Glauner et al. [In German and English.] Cloth. 66 marks; $18.75. Pp. 123, with 205 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

This profusely illustrated book represents a great deal of work on the part of the authors. Each illustration is accompanied by an easily understandable line drawing labeled in detail. The text is in both German and English in parallel columns. The engraving of the illustrations occasionally leaves something to be desired. The world literature on tomography of the temporal bone is reviewed, and the authors describe their own techniques in detail. Hypoclinoid blurring has been produced by the Massiot "Polytome." Methods are presented for taking 1-mm. sections through the temporal bone in six different positions. The normal anatomy of the temporal bone is depicted in 62 illustrations. The remaining films demonstrate a wide variety of lesions, including atresias, fractures, infections, and tumors.

The authors' introduction correctly states that tomography is to be considered an amplification of, not a substitute for, conventional mastoid films taken with good technique in properly chosen positions. Certain lesions, however, especially labyrinthine fistulas and severe congenital atresias, can be examined effectively by the tomographic technique. Although this book may not be of great interest to either the general radiologist or the surgically oriented otologist, it is recommended strongly to those roentgenologists particularly interested in the radiologic examination of the temporal bone.

Röntgendiagnostik des Magen-Darmkanals. Von Prof. Dr. R. Prévôt und Priv.-doz. Dr. M. A. Lassrich. Cloth. 119 marks; $28.30. Pp. 346, with 544 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

It is difficult to review in a comprehensive way the roentgenographic diagnosis of diseases of the gastrointestinal tract, gallbladder, and pancreas. The authors have succeeded admirably in their presentation of this material, avoiding both redundancy and repetition. A wealth of material has been compiled in about 300 pages. The text is adequately and beautifully amplified by the illustrations. It is refreshing to note the emphasis placed on differential diagnosis. The text includes scholarly discussions of such subjects as congenital anomalies, inflammatory and neoplastic diseases, functional disturbances, and localization of foreign bodies. The anatomic and pathological changes associated with each of the conditions have not been overlooked. For particular commendation were the references made to the acute abdomen, especially in the pediatric patients. The "scout film," mucosal pattern demonstrations, and the more recent advances in intravenous cholangiography, as well as their limitations, are here discussed. Brief historical references and a well-documented bibliography round out the volume. This book can be recommended unreservedly not only to radiologists but to any specialist or practitioner who is interested in the roentgenographic diagnosis of gastrointestinal disorders. A good reading knowledge of German is desirable.

QUESTIONS AND ANSWERS

ADVERSE DRUG REACTIONS AND MALPRACTICE

To the Editor:—*Would a physician be liable for malpractice if a patient had an adverse reaction to a drug in a case in which there was no history of previous intake of or reaction to the medicament?*
M.D., Illinois.

Answer.—Adverse reactions to drugs are of two major categories, toxic or allergic. Patients whose tolerance to the pharmacological action of the drug is low may have exaggerated and alarming responses to ordinary moderate doses of the drug. Side-effects unrelated to the drug's therapeutic action are considered toxic effects, such as sedation from antihistamines or overstimulation from epinephrine. Allergic reactions to drugs have no pharmacological basis and are manifestations of altered tissue responses. Urticaria, asthma, anaphylaxis, "serum sickness," thrombocytopenia, and granulocytopenia are examples.

The fact that a patient has a low tolerance can be ascertained only when there is a history of previous reaction from that class of drugs, but administration of normal doses to this type of patient usually causes unpleasant but not serious effects. In a case in which disastrous side-reactions may ensue, it is wise to give a preliminary small dose before the therapeutic dose is given. Whether failure to do this would be considered malpractice or not is questionable and would also depend on the usual custom in the community. The causing of side-effects from approved drugs is usually not a basis for a malpractice suit, unless the physician has been careless in supervising the treatment and observing the patient. For example, undesirable effects may be produced by corticosteroid therapy, but the doctor and the patient must be aware that the side-effects may develop in the patient during this type of treatment for asthma or rheumatoid arthritis. If serious side-effects arise because the drugs are used indiscriminately and without medical supervision, negligence can be claimed. The physician assumes added responsibility when administering new drugs not yet approved for general use.

Generally, the physician cannot be blamed for the allergic effects of a drug if he has avoided the use of potent allergenic drugs, when these were not necessary; inquired about the patient's previous response to the particular drug; made skin tests, where these were applicable; and made preliminary use of a fraction of the dose, when doubt existed. A skin test result is not always dependable, since it may be negative in the presence of allergy. The physician may be held negligent if he bases his opinion of the drug's harmlessness on such negative skin test results. Certain drugs will produce positive results of skin tests and forebode the possibility of the sudden appearance of urticaria, asthma, or anaphylaxis, and some of the most used drugs in this category are penicillin, streptomycin, animal serums, organ extracts (insulin, liver fractions, and pituitary products, including ACTH), enzymes, and other organic and some inorganic preparations. The physician is responsible for knowing this list. The result of a skin test with penicillin or serum is significant only to screen the patients prone to immediate (anaphylactic) reaction, which has no relation to delayed "serum sickness." Malpractice is established on proof of negligence, which is determined by the usual practice among physicians. For example, serum injections are rarely administered without a previous test, and, as the population becomes increasingly sensitive to penicillin, the custom of preliminary skin-testing should become more routine; when it does, failure to make preliminary skin tests may be regarded as negligence.

TREATMENT FOR TAPEWORMS

To the Editor:—*What is the treatment for a patient infested with Taenia saginata? Quinacrine has been used, but apparently the head remains.*
Lloyd H. Murdock, M. D., Zwolle, La.

Answer.—Of the many anthelmintics that have been used to rid a patient of T. saginata quinacrine is the most effective and least toxic. Failure to obtain the head is most often due to inadequate preparation of the patient's intestinal tract before the anthelmintic is given; the fact that the drug is impotent or not fresh, especially when oleoresin of aspidium is used; and the lack of intelligent cooperation by the patient.

The following routine should be used. 1. For two days before treatment the patient should adhere to a light, residue-free diet. 2. The night before treatment the patient takes 1 tbsp. of a saline purge such as sodium sulfate dissolved in a full glass of water. 3. On the day of treatment the patient is kept in bed and receives no breakfast except plain tea or black coffee; 30 mg. of phenobarbital is given one hour before treatment. 4. One hour later the patient receives 0.2 Gm. of quinacrine. Depending on the

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

weight of the patient the same dose is repeated every 10 minutes for four or five doses, until a total of 0.8 to 1.0 Gm. has been given; 0.6 Gm. of sodium bicarbonate is given with each dose of quinacrine to allay nausea. 5. Two hours after the last dose of quinacrine the saline purge is repeated. 6. Save all stools. It is best to collect them in a commode filled with warm isotonic sodium chloride solution, with the patient's anus immersed in the solution so that the worm is passed from the body to the solution, because the cooling and drying effects of the air may cause the worm to break in the region of the slender neck. If the head is retained it will mature in two or three months and the patient will start to pass segments and ova again. 7. Examine all stools. Usually the entire worm, 5 to 25 meters in length and stained deep yellow by the medicament, is passed at one time. Examine the worm. As the head is approached the worm becomes narrower and is thread-like in the region of the neck. The head is wider than the neck, rhomboidal in shape, and usually black. 8. The patient may take food after a copious bowel movement results from the second purge.

When these directions are followed the rate of cure is high. T. saginata infestation is usually single but may be multiple. Man is the definitive host. The adult worm matures and lives in the intestinal tract of man, and proglottids and ova are passed in his stools. The larval stage does not occur in man.

ECLAMPTIC TOXEMIA

To THE EDITOR:—*Please discuss the use of muscle relaxant drugs, particularly succinylcholine, for management of a patient with eclampsia. Would they be more effective than administration of hypertonic solutions of magnesium sulfate or barbiturates in this respect? What is the status of the antihypertensive drugs such as reserpine for control of hypertension in eclampsia? Which anesthetic agent should be given the eclamptic woman during delivery of a viable fetus?*

William S. Skanyd, M.D., Parma, Ohio.

ANSWER.—The administration of curare alkaloids and the synthetic curaremimetic drug succinylcholine is rarely justified in the management of a patient with eclampsia because of the hazard inherent in their use. The muscle components of eclamptic seizures can be alleviated by these agents, but they do not alter the basic abnormalities peculiar to this entity. The margin of safety between therapeutic doses and amounts which will produce diaphragmatic paralysis and hypoxia is narrow. This limits administration of them to physicians who are acquainted with their pharmacological properties and who have the training and facilities for artificial resuscitation by means of endotracheal intubation and continuous positive-pressure respiration. The combined use of magnesium sulfate, antihypertensive drugs, and barbiturates rarely fails to control eclamptic seizures. These drugs have wide margins of safety and are the preferred agents for the management of patients with eclampsia.

A combination of parenterally administered reserpine and hydralazine hydrochloride, which may be supplemented by one of the veratrum alkaloids, is indicated in the management of patients with eclampsia. These agents give effective management of the hypertensive crises and prophylaxis of cerebrovascular accidents which may occur. The antihypertensive drugs are not substitutes for the anticonvulsive action of magnesium sulfate. Many factors influence the choice of anesthesia for a given eclamptic patient. A pudendal block with procaine for vaginal delivery and local infiltration for abdominal delivery afford the smallest risk.

QUADRIPLEGIA AND MEDICAL TRAINING

To THE EDITOR:—*A student suffered a spinal cord injury at the level of the sixth cervical vertebra during the last part of the sophomore year of medical school. He has fair elbow flexion, slight elbow extension bilaterally, and no hand function. Touch perception is present in the skin out to the wrists and in the right thumb. What degree of disability can a student have and still anticipate the completion of medical training?*

Russell E. Youngberg, M. D.
Loma Linda, Calif.

ANSWER.—The prognosis in quadriplegia due to cervical cord injury has changed radically in the past few years. Antibiotics, proper urologic care, and the tilt board for postural management have given adequate medical control of the patients, and with modern self-help devices such patients are able to eat, dress, groom themselves, keep clean, and use an electric typewriter, telephone, or tape recorder. Many quadriplegics have been in competitive business for years. A sophomore medical student should be able to finish schooling if family, fellow students, and faculty cooperate. He should plan to work in some phase of medicine not requiring hand function such as psychiatry, administrative medicine, or medical rehabilitation. Paraplegic and quadriplegic physicians are successfully carrying on active practices today. During consideration of this problem it is fundamental that ability as well as disability be taken into account.

BLOOD FROM CADAVERS

To THE EDITOR:—*Has cadaver blood, such as has been used in Russia, ever been considered an acceptable source of blood in America? This question is often asked when blood centers have difficulty in getting sufficient donors.*

H. W. Garton, M. D., Fort Wayne, Ind.

ANSWER.—Cadaver blood for transfusion purposes attracted some attention in this country (Yudin, S.S.: Transfusion of Cadaver Blood, *J. A. M. A.*

166:997-999 [March 21] 1936) but has never gained acceptance. Objections to its use are (1) a preference for blood from the living donor rather than from the cadaver; (2) the legality of invasion of the body; (3) the difficulties of avoiding bacterial contamination of the cadaver blood (the procedure was restricted, by the Russians, to blood collected within six hours after death and to cadavers of those dying of emergency conditions such as coronary occlusion, cerebral vascular accidents, and severe trauma, since it was believed that such restrictions decreased or avoided the hazard of bacterial contamination); (4) the uncertainty of supply because of (3); (5) the need for stand-by facilities and personnel to collect the blood from suitable and available cadavers; (6) the greater convenience of live donors; and (7) the availability of a history of previous good health from the live donor, serving to protect the recipient. Energies devoted to blood procurement are best applied to the mobilization of living donors. Most treatises on blood procurement ignore the cadaver as a source of blood or merely mention it for historical interest.

WATER SOFTENERS AND LOW-SODIUM DIET

To the Editor:—*Does replacement of the calcium and magnesium ions by the sodium ion take place during the chemical process of softening hard water? Would this be a source of sodium to be calculated when placing a hypertensive patient on a low-sodium diet?*

M. D., Illinois.

Answer.—In some areas water contains in its natural composition sodium chloride in excess of the desired amount for hypertensive patients. The content of sodium in artificially softened water depends on the method of softening used. Large municipalities use the soda-lime type or some modification thereof, and the water is substantially free of sodium. Water treated to "zero" softness is unpalatable, and to overcome this natural water is often added. Smaller city and home units use a method of water softening predicated on ion-exchange. This water has a substantial sodium content, and the harder the natural water the higher the sodium content.

Laubusch and McCammon (*Am. J. Pub. Health* 45:1337 [Oct.] 1955) concluded that water softened by the ion-exchange (zeolite) method might contain more sodium than is desirable for some hypertensive patients. They gave as an example water with an initial sodium content of 387 ppm and a hardness of 1,250 ppm of calcium carbonate; after the cation-exchange process each liter would contain about 960 mg. of sodium (2.44 Gm. of sodium chloride). They stated, "Each situation must be considered individually. Ion-exchange or excess lime soda softening, even of very hard waters having a high initial saline content, would rarely be in any way physiologically harmful to a person in normal health. Except in those cases where the concentration of sodium, as well as of calcium and magnesium ions, in the presoftened water is unusually high, the effects of the additional source of sodium are not insurmountable for ambulatory patients on a less intensive sodium restriction regimen, provided that they are aware of the situation, its significance, its effects, and what might be done to overcome it."

VACCINATION REACTION

To the Editor:—*A one-year-old infant was given typhoid vaccine at the time a smallpox vaccination pustule was forming. He developed fever and convulsions. Can it be assumed that this was due to the concurrent administration of the vaccines? The patient, now aged 3, will be going to Europe next year and needs typhoid immunization. Would you advise the administration of fractionated doses of typhoid vaccine?*

John O. Martin, M.D., Falls Church, Va.

Answer.—It is difficult to determine whether the high temperature was due to the stage of the smallpox vaccination or whether it was precipitated by the typhoid vaccine. It would have been more prudent to have delayed typhoid vaccination until the active stage of the first vaccination had subsided. The dose of the typhoid vaccine (not stated) and the infant's central nervous status, i. e., whether he had cerebral palsy or a tendency to febrile convulsions, are important factors to consider. Since this patient received his basic typhoid immunization at infancy and is now 3 years of age, a "booster" dose of 0.1 cc. of typhoid vaccine administered intradermally should be sufficient. If the attending physician considers that a larger amount is necessary, then fractionated doses of the vaccine are indicated. (See "Report of the Committee on the Control of Infectious Diseases," published by the American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill.)

HYPERGLYCEMIA AND NO GLYCOSURIA

To the Editor:—*How is it possible for a patient to have a blood sugar level of 525 mg.% and no glycosuria, with the specimens having been taken at the same time? The urine was collected by an indwelling catheter. The patient's nonprotein nitrogen level was 110 mg. per 100 ml. The urinary output was below normal.*

E. N. Krueger, M. D., Appleton, Wis.

Answer.—The renal threshold for glucose excretion may be elevated by renal disease, and this possibility is suggested by the increased level of nonprotein nitrogen reported. Glucose excreted in urine depends on the amount of glucose filtered from the blood by the glomeruli and the amount reabsorbed in the renal tubules. Diseases that damage the glomeruli, such as nephrosclerosis or glomerulosclerosis, will decrease or stop glomerular filtration of glucose from the blood, thereby causing hyperglycemia and no glycosuria. When anuria is present, regardless of the cause, much time may elapse before glucose equilibrium is established between the blood and the urine. The blood flow to the kidney is so decreased that the small amount of glucose filtered by the glomeruli is completely reabsorbed by the tubules. Urinary output of less than 400 cc. per day is usually accompanied by high blood sugar levels and little or no sugar in the urine.

In pyelonephritis the tubules are so damaged that glucose reabsorbtion decreases and there is a decrease of blood sugar content. If there is disease of the kidneys one should not depend entirely on the urinary sugar content to indicate the effectiveness of treatment.

PHOTOGRAPHY IN SURGICAL SUITES

To the Editor:—*Is there an ether explosion hazard if photographs are taken in an operating room with use of the available light, a Nikon camera, and high-speed Ektachrome film?*

F. Goldwasser, M.D., Alma, Ga.

Answer.—The Nikon camera and high-speed Ektachrome film used in conjunction with light from surgical lamps and other available room illumination is a nonhazardous method of photography in an operating room. If additional illumination is provided by customary flood lamps or photoflash lights, the bulbs and the power source must be at least 5 ft. above the floor and 3 ft. away from the anesthesia equipment to avoid the possibility of fire from flammable anesthetics.

POLIOMYELITIS VACCINE AND TONSILLECTOMY

To the Editor:—*It has been the practice not to perform tonsillectomies and adenoidectomies during July, August, and September because of the possibility of these patients' developing poliomyelitis. Has the poliomyelitis vaccine altered this situation?*

Donald I. Dean, M.D., Rushville, Ind.

Answer.—The Expert Committee on Poliomyelitis of the World Health Organization considered this problem and concluded that, since the vaccine has no appreciable influence on the excretion of poliovirus in the stool, and since there may be no interference with the growth of the virus in the pharynx, it is advisable to discontinue such elective procedures during the poliomyelitis season. More recently eight prominent virologists expressed a similar opinion. During 1958 in the United States 322 paralytic cases of poliomyelitis and 20 deaths were reported in persons who had received three injections of vaccine. These figures support the recommendation that elective tonsillectomies or adenoidectomies, or both, be postponed during the months when the incidence of poliomyelitis is high. See also "Editor's Column," *Journal of Pediatrics,* May, 1959.

LACTATION DUE TO HYSTERECTOMY

To the Editor:—*Is lactation a common occurrence after a hysterectomy has been performed? Is it of any significance? Is there an etiological relationship?*

Harry L. Clark, M.D., Brooklyn, N. Y.

Answer.—This consultant has heard of lactation taking place after hysterectomy, but such claims have not been validated nor has information about associated procedures that may have been done at same time, such as oophorectomy, been available. Nothing, other than stress, that might influence the factors initiating and maintaining lactation is associated with the operation. The endometrium and the myometrium are influenced by progesterone and estrogen and in turn might influence their utilization, but there is no known relationship between this and the removal of the uterus that might initiate lactation. In answer, it is correct to make the dogmatic statement that lactation is not commonly observed to take place in a woman after a hysterectomy.

SCHICK TEST—DTP—DTPP

To the Editor:—*Should a child who has never received immunization for diphtheria and has a negative response to the Schick test receive three injections of diphtheria toxoid, or will it suffice to give a booster dose?*

Abraham Katz, M.D., Bronx, N. Y.

Answer.—The child who has not received immunization for diphtheria and who shows a negative response to the Schick test should be retested with fresh Schick test material. If the test result remains negative, diphtheria toxoid need not be administered. Most authorities state that such a person has acquired adequate immunity without the primary series of toxoid injection. These persons usually live in congested urban areas, have been exposed to others with subclinical infections of diphtheria, and contact the bacillus in doses too small to cause the disease yet adequate to elicit a protective antibody response.

Triple antigen—a mixture of diphtheria and tetanus toxoids and pertussis vaccine (DTP)—has been widely used in the United States since 1943. Three properly spaced doses of the adjuvant-containing antigen, administered intramuscularly, should protect simultaneously against these three diseases. Zoeller of the Paris Pasteur Institute (C. Zoeller, Bacille diphthérique, in Natan-Larrier, L.: Traité de Microbiologie, Paris, Gaston Doin & Cie, vol. 2, p. 88, 1934) gave evidence that higher and more lasting immunity responses result when toxoid doses are administered farther apart—preferably at four-week to six-week intervals. A booster dose of DTP is advised two or three years later and should be repeated when the child enters school. Reactions are mild when aluminum phosphate is used as an adjuvant. The National Institutes of Health recently released quadruple antigen against diphtheria, tetanus, pertussis, and poliomyelitis (DTPP). Two reputable commercial biological laboratories market it. A periodic booster dose is advised. Local reactions are infrequent and transient. Such systemic reactions as fever occur somewhat more frequently than after administration of DTP, occasionally exceeding 103 F (39.4 C) rectally but usually dropping to normal within 24 to 36 hours, especially after administration of a few doses of aspirin and liberal quantities of water by mouth. Quadruple antigen (DTPP) is not recommended for use in patients over the age of 6 or 7 years, but it confers protection against these four diseases at the earliest age, if started at 3 months of age and administered as directed.

TETANUS TREATMENT AND PROPHYLAXIS

To the Editor:—*In* The Journal, *Aug. 15, page 2036, a sensitivity test involving the intravenous use of tetanus antitoxin is recommended as being safe. This test is new to us, and, since we occasionally receive inquiries from physicians about sensitivity tests for our tetanus antitoxin, we would appreciate information or references on the test.*

Hugh Macdonald, M.D.
Lederle Laboratories
Pearl River, N. Y.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*In the past 35 years, in the Communicable Disease Service, over 26,000 patients with diptheria, 400 to 500 with tetanus, and many with meningococcus meningitis and other diseases requiring serum or antitoxin treatment were cared for prior to the advent of antibiotics. Some time ago the following rules were given about the use of antitoxins and serums.*

Before either is administrated to a patient, a skin test and a control are done and their results compared in 30 minutes. If the result is positive, desensitization is required before the patient receives the serum under test. A negative skin test result is not considered evidence for lack of systemic sensitivity, and the intravenous test is next applied.

The intravenous test is made in the following manner. The patient's blood pressure is taken and recorded; 0.1 cc. of the antitoxin or other serum in question is diluted in 10 cc. of isotonic sodium chloride solution and injected slowly into the patient's vein within 5 minutes; and the patient's blood pressure is then taken and recorded every 5 minutes for 30 minutes. If the blood pressure falls 20 points or more, it is considered best to desensitize the patient before the serum is administered. This method has been changed a little from the original test, but years of experience have shown it to be the safest.

Time is often an essential factor in treating the patient. Should a patient be highly sensitive to tetanus or diphtheria antitoxin, the usual method of desensitizing (repeated administration of small doses at frequent intervals) may be too time-consuming. Intravenous administration of heparin, 20 mg. per kilogram of body weight, will prevent serum reaction and anaphylaxis. It may take up to 18 days for complete elimination of foreign proteins (of antitoxins) from the blood stream; therefore, it is necessary to keep the patients heparinized during that time.

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TETANUS IMMUNE GLOBULIN

To the Editor:—*In* The Journal, *Sept. 5, page 130, a tetanus immune globulin biological substance is referred to. Is this the pooled gamma globulin ordinarily used for the prophylaxis of measles and poliomyelitis or is it a separate biological product?*

Jerome Glaser, M.D.
85 San Gabriel Dr.
Rochester, N. Y.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Tetanus immune globulin is made by Cutter Laboratories of Berkeley, Calif., distributed with the trade name of "Hyper-Tet," and available in California only. It is packaged in 1,500-unit vials for administration by intramuscular injection. Tetanus immune globulin consists of the gamma globulin fraction prepared from venous blood of persons who have been immunized with tetanus toxoid. Administration of it is restricted to patients who are allergic to horse serum and in whom the prophylactic immunizing injection of horse serum tetanus antitoxin might produce an untoward allergic reaction. Pooled gamma globulin, which is used in prophylaxis of measles or poliomyelitis, is not satisfactory, because the antitoxin content is low and insufficient for adequate prophylaxis against possible tetanus infection.*

WASHINGTON NEWS

Drug Price Investigation . .
Social Security Hearings . .
Network Advertising . .
Pilot Age Limit Ordered . .

DRUG HEARINGS OPEN—INDUSTRY DEFENDS PRICES

Drug manufacturers disputed charges by Senate investigators that prices are too high, asserting that they are pegged to finance vital research for new drugs and for necessary safeguard controls on their products.

They made the statements as the Senate antitrust subcommittee headed by Sen. Estes Kefauver (D., Tenn.) opened extensive hearings on the drug industry. The senator said that the purpose of the investigation was to determine whether the industry charged artificially high prices or violated any antitrust laws through intercompany agreements and whether new legislation was needed.

The hearing was part of a series by the subcommittee on major U. S. industries. Previous subjects were the automobile, steel, and bakery industries.

In an opening statement, Kefauver said that it is not the purpose of these hearings to question in any way the American system of private medical practice. "Our interest is simply with the price of drugs—a price which must be paid by someone under any system of medical care," he said.

The first week of the hearings dealt with drugs used to treat arthritis. Spokesmen for the major producers of such corticosteroid drugs—Schering and Upjohn—testified, among other witnesses.

Lead-off witness was Francis C. Brown, Schering president. He declared that charges by Kefauver of huge markups on Schering products were completely misleading and designed for headline purposes.

"Considerably more is involved than discovery and manufacture of new compounds," he pointed out. "For every good compound that is found there are many failures. Some failures come after years of effort and hundreds of thousands of dollars of expense. They may come even as our company is ready to market a product it considers good because some competitor has announced something better."

Brown told the subcommittee that he could name at least half a dozen products on which some $500,000 was spent and with nothing to show for it but the experience. Recently, the company had to abandon a research project that had cost more than $1,500,000, he noted.

The official said his company was in business "not just for today, but for tomorrow," and must continue research through profits and earnings.

"The consumers of today must contribute to the benefits which the future will bring, just as the government expects taxpayers to do," he asserted, adding that "the public cannot afford to hamper research by companies which have advanced the cause of medicine so significantly."

John T. Connor, president of Merck, testified that the drug industry is "highly competitive" and "free of excessive concentration." Both research and profits are necessary, he said, if the hunt for new breakthroughs in the drug field is to continue.

Kefauver announced that after hearing from producers of drugs for treating arthritis, the subcommittee would call officials of companies making insulin, antibiotics, tranquilizers, and sulfonamides. He also said that some physicians would testify on their views about drug costs.

Another witness, Floyd B. Odlum, Chairman of the Arthritis and Rheumatism Foundation, told the subcommittee that as many as 5 million of the 11 million persons in the United States who suffer arthritis buy fake remedies every year. He recommended strong federal curbs to prevent false claims for quack patent medicines for which consumers pay an estimated 250 million dollars a year.

BROAD SOCIAL SECURITY HEARINGS SLATED

A sweeping investigation of proposals for changing the Social Security program was charted for the new congressional session.

The hearings were announced by chairman Wilbur Mills (D., Ark.) of the House Ways and Means Committee. He did not say whether the controversial Forand bill to finance medical and hospital care for the elderly through Social Security would be taken up.

Mills said that due to many inquiries and the general interest in this subject he felt the committee would want to develop an agenda on Social Security revision.

He said it appears that "some improvements can be made . . . without necessitating an increase in the existing schedule of contributions rates by employers and employes, and the self-employed." The Forand bill, of course, would require further increases in the tax rates, with estimates of some $2 billion annually.

Many of the suggested changes advanced by Mills for consideration involved a liberalization of the disability program under which totally disabled

(Continued on next page)

persons aged 50 years and over receive Social Security benefits. One of the proposals would eliminate the age requirement of 50 years and open the program to beneficiaries regardless of age. Rep. Burr Harrison (D., Va.), chairman of a ways and means subcommittee that held hearings on the disability program earlier this year, has already announced that he would introduce a bill to accomplish this.

Removal of the requirement of a six-month waiting period before benefits can be paid again in cases where the disabled person, who has unsuccessfully tried to return to work, comes back on the disability insurance rolls.

Extension of the 12-month trial work period for persons drawing disability insurance benefits to include all types of rehabilitation programs, rather than limiting such rehabilitation programs to those administered by the federal or state governments.

Possible changes in the insured status requirements so that persons now reaching retirement age or who have already reached retirement age will be able to qualify for insurance benefits with fewer quarters of coverage than is now required by existing law.

Payment of monthly insurance benefits to wives and widows who are permanently and totally disabled.

Extension of coverage to various groups which have indicated a desire to be included in the insurance program.

Correction of minor inequities and administrative matters that have been brought to the attention of the committee.

Mills said that among changes which have been suggested which the committee may want to consider but which would require some increase in the existing schedule of contributions rates are the following: first, an across-the-board increase in monthly benefit payments, including modifications in minimum and maximum benefits; second, the addition of new types of insurance benefits; and third, an increase in widows' benefits.

No date was announced for the hearings.

NETWORKS HEALTH-MEDICINE ACTIVITIES PRAISED

The Federal Communications Commission heard a spokesman from the American Medical Association urge that the radio-television industry be given an opportunity to correct any abuses on its own rather than have the federal government move in.

"We feel that our experience in the past eight years with the National Association of Broadcasters, the networks, local stations, and other representatives of the industry have shown that they are sincere in their desire to improve the quality of both programs and commercials in the medical field," said Dr. Eugene F. Hoffman, co-chairman of the A. M. A.'s Physicians Advisory Committee on Television, Radio, and Motion Pictures.

The testimony was part of the FCC's investigation of radio-television practices, including rigged quiz shows, payoffs to disk jockeys, and payoffs for "hidden" advertising—the mention of products or companies on programs sponsored by other advertisers.

Dr. Hoffman, who confined his testimony to the medical-health field, said "it has been the experience of the A. M. A. that the broadcasting industry has been anxious that program material be factually correct and in good taste.

"In your study of radio and television programming, the A. M. A. would like to go on record as complimenting networks and local stations alike for ably and conscientiously devoting time and talent to the dissemination of health information to the general public.

"In the nearly four years that the Physicians Advisory committee has been in existence, it has followed through on more than 200 queries from the broadcast industry," the witness told the commission. "And the industry has been most cooperative in revising scripts—sometimes at a tremendous cost—so that the general public would have correct medical information."

Dr. Hoffman reviewed the A. M. A.'s efforts to have medical and health matters properly presented in films and broadcasting, and pointed out that in 1957 the A. M. A.'s House of Delegates criticized radio-television advertising of "patent medicines" and recommended a more careful screening. He also told the FCC about the A. M. A. state and local society programs to cooperate with stations desiring expert knowledge and opinion on advertising and programs in the field.

"The medical profession—both on a national and local level—stands ready to assist the networks and individual stations in determining accuracy and good taste of broadcast material involving health or medicine—either commercial or public service," Dr. Hoffman said.

SIXTY-YEAR AGE LIMIT SET FOR PILOTS

The Federal Aviation Agency has placed a 60-year age ceiling on airline pilots, to go into effect March 15. The order was immediately challenged by the Air Line Pilots Association, which contended that it would in no way improve air safety.

However, FAA Administrator E. R. Quesada said the move was necessary to assure the highest possible degree of public safety in an era when huge jet planes carry up to 165 passengers at 550 miles an hour.

The Air Transport Association, representing the industry, called the step "reasonable and judicious."

The Aviation agency postponed action on a proposal for a 55-year age maximum for pilots of commercial jets and scheduled a public hearing on this for Jan. 7. Both the industry and pilots organizations opposed the lower jet pilot age requirement.

S. N. Sayen, president of the pilots group, commented that "in all of our lengthy study over a period of many years, we have been unable to uncover evidence of a need for such a rule. He said it would cut the earnings powers of pilots who are physically capable of flying although over the age of 60 years.

Advertisement

Pro-Banthīne®...what it will do and what it will not do...in Peptic Ulcer

Much consideration has been devoted recently to a reappraisal of the role of anticholinergic drugs in the management of peptic ulcer.

Such reappraisal has presented no difficulties at Searle. At no time have we suggested that Pro-Banthīne should be substituted for antacids, rest, psychotherapy or even common sense in managing the patient with peptic ulcer.

Action of Pro-Banthīne:

The action of Pro-Banthīne (brand of propantheline bromide) is simple and its effects, allowing for the variability of the human estate, are predictable. Pro-Banthīne competes with and, in competing, inhibits the action of acetylcholine. This competition is highly effective at parasympathetic effector sites and, except with high dosage, somewhat less so at the autonomic ganglia.

Since parasympathetic nerves are motor and secretory to the stomach and motor to the intestines, Pro-Banthīne reduces both motility and secretions in the stomach and motility in the intestines. These actions have often been demonstrated experimentally and clinically.

What It Does:

Relieves Pain—One of the natural consequences of the actions of Pro-Banthīne is to reduce or to eliminate pain in peptic ulcer. Whether the pain is attributable to acid, to excessive motility or, to steer a middle course, to spasm induced by acid, the pronounced inhibitory effect of Pro-Banthīne on both secretion and motility might be expected to suppress the characteristic distress of ulcer.

In point of fact, relief of pain is one of the most prominent effects of Pro-Banthīne in peptic ulcer. Phrases such as "unexcelled" and "almost invariably effective" dot the literature referring to it.

Reduces Acidity—Since reduction of acid and rest for the hypermotile stomach and duodenum are accepted means of supporting the regenerative processes of the gastroduodenal mucosa, the physiologic modifications induced by Pro-Banthīne should be expected to have therapeutic implications in the healing of ulcers also. They do. Not only does Pro-Banthīne reduce gastric acid and motility but, through these actions, it also potentiates and prolongs the neutralizing property of antacids.

Aids Healing—Schwartz, Lehman, Ostrove and Seibel prescribed 120 to 180 mg. of Pro-Banthīne daily for 129 ulcer patients and found definite evidence, both clinical and roentgenographic, of accelerated healing.

With high doses (270 to 330 mg. daily) Barowsky, Schwartz and Lister reduced the mean duration of treatment in twenty-five patients with refractory ulcers from 135 to 17 days.

Helps Prevent Recurrences—Much the same considerations argue for the value of Pro-Banthīne in holding the reactivation of healed ulcers in abeyance, but the difficulty of regulating the diet, medication and mode of living of ulcer patients over long periods of time makes assessment of the role of Pro-Banthīne in preventing recurrences difficult. Nevertheless, in a study of 250 patients with established patterns of recurrence Texter and associates found that patients maintained on methantheline, less potent analogue of Pro-Banthīne, had significantly fewer recurrences than a control series taking atropine.

Schwartz and his co-workers considered freedom from symptoms when recurrences would be expected, together with tolerance and relief of symptoms, as a standard in establishing successful treatment in 118 of 129 patients.

Provides Selective Action—In inhibiting the action of acetylcholine in the stomach and intestines Pro-Banthīne also, though to a lesser extent, influences other cholinergically activated organs. That this influence sometimes leads to such secondary effects as dryness of the mouth, blurring of vision and hesitancy of urination is well known and bears consideration. It is one of the distinct advantages of Pro-Banthīne that it acts more effectively on the gastrointestinal tract than elsewhere. Secondary effects usually disappear during the course of treatment and only rarely limit therapy.

Evidence of selective action has been recorded by several investigators, but the most interesting confirmation of this selectivity was reported by Barowsky, Schwartz and Lister. They prescribed 30 to 45 mg. of Pro-Banthīne every hour and a half, except for the hour before and the hour following meals, for their patients with refractory ulcers. They were surprised and gratified by how few anticipated side reactions materialized. No serious toxic effects or side reactions occurred. The incidence of good response on double or triple the usual doses rose from 31 to 88 per cent.

Lowers Incidence of Failures—Variable results might be anticipated in a disease in which the psychic component plays such a large part and, of course, response to treatment does vary in patients with peptic ulcer. Observations of Lichstein and associates show that the 11 per cent of their patients who failed to respond to Pro-Banthīne had deeply ingrained anxiety on a psychoneurotic basis.

Successful management of such patients may well depend more on the patient's intelligence, the modification of his social environment and the skill of his physician in psychotherapy than on any medication. However, the successful experience of Barowsky and his colleagues in using large, frequent doses of Pro-Banthīne in patients with refractory ulcers might be borne in mind before Pro-Banthīne is abandoned as ineffective. Also worthy of trial in these patients is Pro-Banthīne® with Dartal® (brand of propantheline bromide with thiopropazate dihydrochloride), which combines the outstanding anticholinergic action of Pro-Banthīne with the highly efficient tranquilizing action of Dartal.

What It Will Not Do:

There are aspects of the medical management of peptic ulcer in which Pro-Banthīne has no demonstrable benefit. There is no reliable evidence that Pro-Banthīne reduces the incidence of complications or the need for surgery.

It will not abolish the obligation of physicians to evaluate each patient individually and to modify therapeutic measures to each patient's requirements. Nor will it do away with the necessity for the patient to regulate his life to the demands of his disease. But the modifying action of Pro-Banthīne on the physiologic activity of the gastrointestinal tract and its beneficial effects on the course of peptic ulcer have been established by too many investigators to be seriously questioned. Wisely used in conjunction with other standard therapeutic measures, Pro-Banthīne can inhibit pain, hasten healing and space out the intervals of peptic ulcer recurrence and do so without serious discomfort to the patient.

G. D. Searle & Co., Chicago 80, Illinois.
Research in the Service of Medicine.

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Lichstein, J.; Morehouse, M. G., and Osmon, K. L: Pro-Banthine in the Treatment of Peptic Ulcer. A Clinical Evaluation with Gastric Secretory, Motility and Gastroscopic Studies. Report of 60 Cases, Am. J. M. Sc. *232*:156 (Aug.) 1956.

Schwartz, I. R.; Lehman, E.; Ostrove, R., and Seibel, J. M.: A Clinical Evaluation of a New Anticholinergic Drug, Pro-Banthīne, Gastroenterology *25*:416 (Nov.) 1953.

Sollman, T.: A Manual of Pharmacology, ed. 8, Philadelphia, W. B. Saunders Company, 1957, p. 399.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

December

American Association for the Advancement of Science, Morrison Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. of Virginia, Richmond, Va., Director of Public Information.

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Mid-Winter Clinical Convention for Ophthalmologists and Otolaryngologists (29th), Research Study Club, Ambassador Hotel, Los Angeles, Jan. 17-22. Dr. Norman Jesberg, 500 S. Lucas Ave., Los Angeles 17, Secretary-Treasurer.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, I [illegible] Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. [illegible] Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-Presi[illegible].

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz., Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel, Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago, Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-Treasurer.

American Academy of General Practice, Philadelphia, Mar. 19-24. Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, Mo., Executive Director.

American Association for the History of Medicine, Inc., Charleston, S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Institution, Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broadmoor, Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Portland Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, New Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ. of Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. 30. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Treasurer.

American Laryngological Association, Deauville Hotel, Miami Beach, Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of Technology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Society, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Fla., Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minneapolis 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, Montreal, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, N.Y. Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Rico, Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory University, Atlanta 22, Ga., Secretary.

Missouri State Medical Association, Sheraton-Jefferson Hotel, St. Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Louis 3, Executive Secretary.

National Health Council, National Health Forum, Miami, Fla., Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, Executive Director.

National Multiple Sclerosis Society, New York City, Mar. 8. Mr. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Mar. 30-Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimore 1, Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel, New Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave., New Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, Mar. 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Executive Secretary.

Southwestern Surgical Congress, Riviera Hotel, Las Vegas, Nev., Mar. 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma City, Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral Semmes Hotel, Mobile, Apr. 21-23. Mr. W. A. Dozier Jr., 19 S. Jackson St., Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla., Apr. 25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Executive Secretary.

American Association of Anatomists, Statler-Hilton, New York City, Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Medicine, Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Immunologists, Chicago, Apr. 11-15. Dr. Calderon Howe, Columbia Univ. College of Physicians and Surgeons, New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists, Hotel Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. Holman, Dept. of Pathology, L. S. U. School of Medicine, New Orleans, La., Secretary.

American Association of Railway Surgeons, Drake Hotel, Chicago, Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Executive Secretary.

American College of Obstetricians and Gynecologists, Netherland Hilton Hotel, Cincinnati, Apr. 2-6. Mr. Donald F. Richardson, 79 W. Monroe St., Chicago 3, Executive Secretary.

American College of Physicians, Mark Hopkins & Fairmont, San Francisco, Apr. 4-9. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

American College of Surgeons, Sectional Meeting, Hotel Leamington, Minneapolis, Apr. 11-13. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Kahler Hotel, Rochester, Minn., Apr. 14. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Dermatological Association, Inc., Boca Raton Hotel, Boca Raton, Fla., Apr. 8-12. Dr. Wiley M. Sams, 308 Ingraham Bldg., Miami 32, Fla., Secretary.

American Physiological Society, Chicago, Apr. 11-15. Ray G. Daggs, D.Sc., 9650 Wisconsin Ave., Washington 14, D. C., Executive Secretary.

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NONTROPICAL SPRUE

FUNCTIONAL EFFICIENCY OF SMALL INTESTINE AFTER PROLONGED USE OF GLUTEN-FREE DIET

Paul A. Green, M.D., Eric E. Wollaeger, M.D., Harold H. Scudamore, M.D.
and
Marschelle H. Power, Ph.D., Rochester, Minn.

Ten patients who had nontropical sprue but had been kept relatively free from symptoms by adhering to a gluten-free diet were studied with respect to the functional capabilities of the small intestine. The gluten-free diet is known to improve the nutritional status, but the improvement has not been accepted as denoting complete recovery. The laboratory and roentgenographic findings in this series indicated general improvement of intestinal function, but none of the patients had completely normal digestion and assimilation. The most consistent abnormal finding was steatorrhea both before and during the investigation. Azotorrhea persisted in two patients, and abnormal tolerance curves for glucose and vitamin A were present in eight. The fundamental intestinal disturbances, other than gluten intolerance, that cause nontropical sprue remain to be determined.

IT IS now established that many patients who have nontropical sprue achieve virtually complete relief from the symptoms of their disease when treated with a gluten-free diet.[1] In these instances lost weight is regained, energy returns, and diarrhea subsides. Such improvement in the clinical state is associated with betterment of the hematological and biochemical pictures and, in many instances, with return to a normal roentgenologic appearance of the small intestine. These favorable changes presumably reflect increased efficiency of intestinal function brought about by means of the special diet.

It has not been clearly settled whether recovery of this function is complete after such induced remissions. Some published studies[1] indicate that the absorption of fat returns to normal, which suggests that abnormalities of other intestinal functions also may be corrected. However, other contributions suggest that intestinal absorption may remain impaired despite good clinical remissions. In support of the latter belief has been the observed persistence in some cases of the following features: steatorrhea[2]; flat tolerance curves after oral admin-

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From the Mayo Clinic and Mayo Foundation. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

Read before the Section on Gastroenterology and Proctology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 11, 1959.

istration of glucose,[3] vitamin A, and xylose[2b]; impaired absorption of folic acid,[4] vitamin B_{12},[5] and iron[3]; roentgenologic evidence of a deficiency pattern[6]; and abnormal jejunal mucosa obtained by intubation biopsy.[7]

The evidence just mentioned that points to persistence of malabsorption after gluten-free dietotherapy has seldom been emphasized, since principal attention has been given to the favorable clinical response. Most such studies have been carried out after relatively brief or unstated periods of treatment, at which time maximal improvement of intestinal function may not yet have occurred. Under such circumstances, there naturally would be reluctance to emphasize the incompleteness of the return to normal intestinal function.

Our experience has caused us to wonder whether such recovery is ever really complete even after long periods of successful use of a gluten-free diet. The answer to this question appeared to be important for two reasons. First, if evidence of malabsorption persists during such treatment, the possibility then remains that intolerance to gluten is not the ultimate cause of the disease and that the deleterious effect of administration of gluten is superimposed on some other underlying abnormality. Second, persistence of malabsorption, if it occurs, signifies that states of nutritional deficiency may develop unless appropriate supplements are added to the therapeutic regimen.

Therefore, we decided to assess the efficiency of intestinal function in a group of patients with sprue who had entered prolonged clinical remissions induced by treatment with the gluten-free diet. The results of this study gave evidence of persistent malabsorption in every case.

Patients Studied

The series included 10 patients who had primary (or *idiopathic*) *nontropical sprue* and who returned for this study at our request. They were selected primarily because they had experienced prolonged and apparently complete remissions after removal of all wheat and rye gluten from their diets. In most patients these remissions had been maintained for longer than a year, several having extended to two years at the time of study. In all instances, remissions began within a few weeks after use of the gluten-free diet was started.

All patients were known to have had symptoms of sprue for at least five years prior to the time of the present study, and all had undergone assessment of their condition at the Mayo Clinic one or more times before treatment with the gluten-free diet was begun. They presented the characteristic clinical, laboratory, and roentgenologic features of this disorder. In all patients, the presence of diseases capable of producing a secondary sprue syndrome had been excluded by prolonged observation, repeated clinical examinations, and appropriate laboratory studies. All patients had experienced debilitating exacerbations characterized by fatty diarrhea, abdominal distention, and loss of weight. At some time in the course of their illness they were found to have one or more states of nutritional deficiency; edema caused by hypoproteinemia had existed in four cases, macrocytosis and osteomalacia in five each, and hemorrhagic disorders owing to deficiency of vitamin K in four. A roentgenologic deficiency pattern of the small intestine had been demonstrated in every case, and steatorrhea was shown to be present in all instances by means of quantitative tests for the fecal excretion of fat.

All patients had been treated by conventional methods, and two had also taken cortisone. The details of these therapeutic regimens have been published previously.[8] Failure of such treatment to produce good remissions in these patients led to employment of a gluten-free diet.

Table 1.—*Clinical Data in Patients with Sprue Treated with a Gluten-free Diet*

Case	Age, Yr., and Sex	Duration of Symptoms, Yr.	Time on Gluten-free Diet, Yr.	Weight Gained, Lb.
1	44,F	8	1½	20
2	32,M	32	½	15
3	43,F	43	3¾	15
4	43,M	5	2	40
5	44,M	13	2	25
6	31,M	31	1	20
7	61,F	61	2	35
8	48,M	48	2	20
9	55,F	5	1¼	20
10	61,M	61	1	60

At the time of the present study, 9 of the 10 patients had been taking this special diet for one year or longer, the 10th patient having taken it for six months. The diet employed was free of wheat and rye, but oats were not excluded except in one patient (case 2).

In addition to the gluten-free diet, several patients were taking supplemental doses of minerals or vitamins. Calcium lactate was used in cases 1 through 4, 7, and 10; a water-soluble vitamin D preparation was given in cases 1, 3, 4, 6, 7, and 10; a water-miscible vitamin K preparation was given in cases 1, 4, 6, 7, and 10; multiple-vitamin capsules were given in cases 1, 2 through 7, and 10; and parenteral injections of vitamin B_{12} or liver extract were given in cases 4 and 10.

Further pertinent clinical data concerning this group are given in table 1. Of the 10 patients, 6 had experienced symptoms dating back to childhood and no doubt represented examples of celiac disease that persisted into adult life. This incidence of previous celiac disease is greater than that found in a large series of sprue patients who were not chosen on the basis of response to the gluten-free

diet.[9] A history of celiac disical and electrophoretic
in the remaining four cases; tm all patients. When
the opinion expressed by Frenche concentration of
that obvious grounds do not exist for ml. of serum in
improvement in adulthood is limited tment values,
have had the illness in childhood. 0 patients
tion of
Gm.)

Procedures and Methods

A clinical appraisal of each patient was carried out, including a complete medical history and physical examination. Particular attention was paid to details of dietary intake and to persisting symptoms.

The studies were carried out in a metabolic study unit. All patients underwent intake-excretion studies of fat, as well as assessment of the fecal excretion of nitrogen. Collection of stools was supervised by nurses trained in the techniques of balance studies. In each case, the study was preceded by an adjustment period of at least four days during which the patient was maintained on the test diet. During the period of known dietary intake, stools were collected and pooled for six days, the beginning and termination of the period being indicated by ingestion of carmine markers. Analyses were made for the entire period, and the daily values for fecal fat and nitrogen were obtained by averaging. The method used to determine the fat content of the feces was that described by Van de Kamer and co-workers,[10] modified to include all substances extractable into petroleum ether; in other words, essentially total lipids. The values for total lipids obtained by this method are in close agreement with those obtained by the procedure that we formerly employed.[11] Fecal nitrogen content was determined by the Kjeldahl procedure.

In addition to the intake-excretion studies, tolerance tests for orally taken glucose and vitamin A were performed in nine cases. In preparation for the latter procedure, each patient received preliminary doses of vitamin A for at least four days; the daily dose during this period was 50,000 I. U. of vitamin A given in the form of an aquasol, or water-miscible preparation.

Additional methods of assessment in most cases included the following procedures: estimation of the absorption of radioactive cobalt (Co^{60})-labeled vitamin B_{12} by the urinary-excretion method of Schilling [12]; roentgenologic examination of the small intestine after oral administration of a barium sulfate suspension; measurement of total serum protein levels; determination of the albumin-globulin ratio (by the Howe salting-out method) and the sodium and potassium (with use of a flame photometer), inorganic phosphorus, calcium (precipitated as oxalate from ashed plasma), iron, alkaline phosphatase, carotene, plasma cholesterol, phospholipids, fatty acid, and total lipid levels; leukocytes (range of 5,400 to 10,000 per cubic millimeter). Although the classic picture of macrocytosis was not encountered on examination of stained blood smears, the diameter of the erythrocytes measured $8\ \mu$ in two patients (cases 8 and 10).

Comment

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and ability to work full time. Bowel t for a few
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usually were normal in form and color. tention

Despite the observed over-all improvement, certain clinical features remained in a few patients to suggest that impaired function of the small intestine persisted; in 2 of the 10 patients the stools were at times bulky and light in color; 4 patients experienced mild abdominal bloating; 5 noted this symptom and also looseness of the stools unless they restricted the fat content of their diet; 2 had these same symptoms unless they avoided excessive physical fatigue; and 4 had nocturnal diuresis, although it was not severe.

Intestinal Function.—Although, in general, laboratory and roentgenologic studies indicated improvement of intestinal function in all patients, evidence existed that recovery of this function was not complete in any of the patients studied. The values that reflect this persistent impairment in intestinal function are given in tables 2 and 3 and are discussed in the following paragraphs.

Persistence of Steatorrhea and Azotorrhea: Values for fecal fat content obtained during treatment with the gluten-free diet are contrasted with pretreatment values in table 2. The daily quantity of fecal fat during treatment was determined when the dietary intake of fat was 113 Gm. per day, whereas that before treatment was measured when the fat intake ranged from 55 to 100 Gm. per day. Therefore, these two sets of values are not strictly comparable. In both instances, however, we considered that a value for fecal fat in excess of 7.5 Gm. per 24

by the results of both chemical and electrophoretic studies, which were obtained on all patients. When the former procedure was used, the concentration of albumin exceeded 3.5 Gm. per 100 ml. of serum in every case; this contrasts with pretreatment values, which had been decreased in 7 of the 10 patients (range of 2.4 to 3.3 Gm.). The concentration of total globulin was normal (more than 2.0 Gm.) in seven patients but was decreased in the remaining three (1.0, 1.7, and 1.8 Gm. respectively). In most patients, these values were not significantly different from those observed before treatment.

Electrophoresis showed the level of albumin to be slightly depressed in 9 of the 10 patients (range of 2.6 to 3.4 Gm.). The various globulin fractions were not significantly altered except in the aforementioned patient with hypogammaglobulinemia, in whom the level of gamma globulin was only 0.28 Gm. per 100 ml. in contrast to a normal value of 0.8 to 1.6 Gm. Even so, this represented a substantial increase over the initially observed value of zero. This increase occurred despite the fact that the patient had not received parenteral supplements of gamma globulin during the preceding several months. A detailed account of this case, including the possible significance of the increase in gamma globulin during treatment, has been written by Huizenga and associates.[15]

Serum Electrolytes and Minerals: Normal values for serum sodium, potassium, and phosphate contents were observed in every patient. The level of calcium was low (8.5 mg. per 100 ml.) in only one instance. The value for iron was modestly depressed (range of 50 to 76 mcg. per 100 ml.) in four of eight patients tested.

Other Blood Studies: Normal values were obtained in all patients for alkaline phosphatase content and prothrombin time. The level of carotene was extremely low (6.0 I. U. per 100 ml.) in the patient in case 2; borderline low values of 60, 69, and 50 I. U. were found in the patients in cases 1, 7, and 10 respectively. Normal values ranging from 100 to 185 I. U. coexisted with steatorrhea in the other six patients. This latter observation suggests that determination of serum carotene content may be unreliable as a screening test for steatorrhea when the degree of steatorrhea is slight or when the patient tested is in a substantially normal state of nutrition.

Values for total plasma lipids as well as for phospholipids and fatty acids were essentially normal in all instances. In two patients, however, the cholesterol level was low (105 and 128 mg. per 100 ml. respectively).

Hematological Picture.—Normal values were present in every patient for hemoglobin (range of 12.3 to 16.7 Gm. per 100 ml.), erythrocytes (range of 4,110,000 to 5,190,000 per cubic millimeter) and leukocytes (range of 5,400 to 10,000 per cubic millimeter). Although the classic picture of macrocytosis was not encountered on examination of stained blood smears, the diameter of the erythrocytes measured 8 μ in two patients (cases 8 and 10).

Comment

The apparently complete clinical remissions attained by treatment with the gluten-free diet in our patients were not accompanied by full recovery of intestinal function even after extended periods. This is indicated by the observations that steatorrhea persisted in all patients and that flat tolerance curves and a roentgenologic deficiency pattern remained in most patients, despite treatment carried out for more than a year in all but one and in some instances for two years or longer. Our findings thus substantiate the published but usually unemphasized data cited earlier indicating that a measurable degree of malabsorption remains despite the excellent clinical remissions induced by a gluten-free diet.

Several possible explanations exist to account for the persistence of malabsorption observed in our patients. First, the patients may have failed to comply with the prescribed treatment. Four of them purposely had violated the diet for a few periods of one or two days each, but the resultant symptoms of diarrhea and abdominal distention promptly induced them to resume and strictly continue its use; the remaining six patients asserted that they had made every effort to exclude wheat and rye from their meals at all times. That these patients as well as the other four complied with the prescribed diet, with the exceptions noted, is indicated by the fact that they had excellent symptomatic remissions. Second, the small amount of gluten contained in cereals other than wheat and rye that were allowed in the diet may have exerted a harmful effect. In this regard, oats have been considered suspect in cases of celiac disease[16] but their role in sprue in adults has not been finally evaluated.[16] In our single patient from whose diet oats had been excluded, the degree of malabsorption was equivalent to or even exceeded that observed in the other patients. Third, the impairment of absorption may have been perpetuated by injurious dietary agents other than gluten or its constituents; however, to our knowledge, no such agent or agents have been identified so far. In this connection, a number of patients with nontropical sprue observed by us[9] and others[1] have failed to attain even clinical remissions by use of the gluten-free diet. Therefore, it is possible, as some authors suggest, that multiple factors are capable, to a varying extent, of contributing to the abnormal intestinal function in sprue. Finally, the absorptive defect may have a fundamental part of the disease itself, not eliminated by removal of gluten.

hours or of more than 30% of fecal solids confirmed the existence of steatorrhea. It will be noted that values obtained during treatment with the gluten-free diet gave evidence of persistent steatorrhea in every patient.

Table 2.—*Fecal Excretion of Fat and Nitrogen in Patients with Sprue Before and During Prolonged Gluten-free Dietotherapy*

	Intake of Fat in Relation to Gluten-free Diet, Gm.		Fecal Excretion					
			Fat				Nitrogen Gm. per 24 Hr.	
			Gm. per 24 Hr.		% of Solids			
Case	Before	During	Before	During	Before	During	Before	During
1	...	113	17.0	12.5	24	38	7.5	2.0
2	100	113	28.5	61.5	50	64	3.9	4.2
3	55	113	10.5	21.5	14	47	...	2.1
4	100	113	12.0	15.0	37	29	2.2	2.2
5	70	113	32.0	28.5	51	58	...	2.3
6	70	113	23.0	14.5	39	25	4.4	4.7
7	...	113	...	32.0	45	51	...	2.4
8	"Regular"	113	46.0	8.5	62	21	2.2	2.3
9	"Regular"	113	21.5	9 5	44	30	2.0	2.0
10	100	113	63.0	31.0	43	50	9.9	3.0

A value for fecal nitrogen content in excess of 3 Gm. per day was considered to indicate azotorrhea. Such an abnormality was demonstrated during treatment in 2 of the 10 patients studied. In both of these patients, azotorrhea also had been observed previously. The normal values obtained in the other eight patients could be ascribed to gluten-free dietotherapy in only two instances, since the previous levels had been either normal or not determined in the remaining six patients.

Flat Tolerance Curves During Treatment: In five of the nine patients tested, evidence of a flat glucose-tolerance curve was obtained when the maximum value for blood sugar failed to increase by 40 mg. per 100 ml. above the value with the patient fasting; the greatest increments in these five patients ranged from 17 to 22 mg. Previous glucose-tolerance tests had not been performed on these five patients, but it was assumed that these flat curves existed before treatment. In the remaining four patients, the curves were normal; however, pretreatment values, which were available in all four, indicated that only two of these normal curves could be ascribed to treatment, since the other two curves had been normal previously.

A test for absorption of vitamin A was done during treatment in nine patients. In seven of these, the plasma curves were considered to be flat, since the maximum increase of plasma vitamin A content was less than 850 I. U. per 100 ml.[1b] (range of 150 to 805 I. U. per 100 ml.). Thus, results of these tolerance tests provided further evidence of persistent malabsorption in most patients.

Impaired Absorption of Co^{60}-Labeled Vitamin B_{12} During Treatment: By means of the Schilling test, Bull and associates [13] found that normal persons excreted in their urine from 8 to 38% of an oral dose of Co^{60}-labeled vitamin B_{12} during the first 24 hours. Values in this normal range were found during treatment in seven of the nine present patients so treated, which is a significantly greater incidence than that observed in sprue patients not taking a gluten-free diet.[14] Although such tests were not done before treatment, it appears likely that the high incidence of normal absorption of vitamin B_{12} in our patients was related to use of the gluten-free diet. Even so, impaired absorption of this vitamin was encountered in the remaining two patients. In this connection, Frost and co-workers [5] noted an actual decrease in the efficiency of absorption of vitamin B_{12} in a patient with sprue who had been successfully treated with the gluten-free diet.

Persistence of Roentgenologic Deficiency Pattern: In three of the nine patients thus examined, the roentgenologic deficiency pattern observed before treatment with the gluten-free diet was not seen during the present study. A deficiency pattern persisted in the remaining six patients, although in three it was less pronounced during treatment than previously.

Nutritional State.—In contrast to the measurements just presented, those which follow bear primarily on the existence of nutritional deficiencies and only secondarily on the presence of malabsorption. When abnormal, these values may be altered and often corrected by administration of appropriate nutritional supplements. Among our patients, the values obtained were normal in most instances. However, many of the patients had been receiving supplemental doses of vitamins and minerals. Therefore, it is impossible to ascribe the normal nutritional state to the gluten-free diet alone.

Table 3.—*Laboratory and Roentgenologic Evidence of Malabsorption in Patients with Sprue After Gluten-Free Dietotherapy*[*]

Case	Steatorrhea	Azotorrhea	Flat Glucose-Tolerance Curve	Flat Vitamin A-Tolerance Curve	Abnormal Schilling Test Result	Deficiency Pattern
1........	+	0	+	+	0	+
2........	+	+	+	+	0	+
3........	+	0	0	+	0	+
4........	+	0	+	0	NT	+
5........	+	0	0	+	0	+
6........	+	+	0	0	0	+
7........	+	0	+	+	+	0
8........	+	0	+	+	0	0
9........	+	0	0	+	+	0
10........	+	0	NT	NT	0	NT

[*] Present: +; absent: 0; not tested: NT.

Serum Proteins: Except in a single patient with severe hypogammaglobulinemia who was included in this group, the serum concentrations of both albumin and globulin were either normal or only slightly reduced in all patients. This was exemplified by the results of both chemical and electrophoretic studies, which were obtained on all patients. When the former procedure was used, the concentration of albumin exceeded 3.5 Gm. per 100 ml. of serum in every case; this contrasts with pretreatment values, which had been decreased in 7 of the 10 patients (range of 2.4 to 3.3 Gm.). The concentration of total globulin was normal (more than 2.0 Gm.) in seven patients but was decreased in the remaining three (1.0, 1.7, and 1.8 Gm. respectively). In most patients, these values were not significantly different from those observed before treatment.

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Our findings do not establish such a concept but render it tenable. If such an irreversible defect does exist, it is possible, as some observers believe,[4] that it is enzymatic in nature.

Our findings do not detract from the value of a gluten-free diet in the management of certain cases of nontropical sprue. On the contrary, the improved clinical and laboratory pictures encountered among our patients confirm its worth. However, the observed failure of intestinal function to return completely to normal in the period covered by our study merits emphasis. It is possible that this residual degree of malabsorption may lead eventually to further deficiency states. To obviate such a possibility, we have continued to employ supplemental doses of vitamins and minerals in the diets of most patients when the gluten-free diet is prescribed. This has been done even when no evidence of a deficiency state exists and even though the patient has carefully followed the gluten-free diet.

Since this special diet imposes considerable restriction on the patient and entails the use of special recipes for wheat and rye substitutes, we reserve its use for those patients who do not respond well to conventional treatment. The latter regimen enables about two-thirds of the patients with sprue to achieve satisfactory remissions of the disease.[9] Many of these patients prefer to continue use of this conventional program rather than to accept the restrictions imposed by the gluten-free diet.

The most consistent abnormal finding in our patients was steatorrhea. The most reliable method for demonstrating its existence, in our experience, has been the quantitative analysis of feces by means of intake-excretion studies. Such studies indicate that we have not found any form of treatment, including the gluten-free diet, that brings about a complete and permanent return of intestinal function to normal in patients with nontropical sprue.

Summary

Ten patients who had nontropical sprue were selected for study at the Mayo Clinic on the basis of their prolonged and apparently complete clinical remissions of the disease after treatment with a gluten-free diet. Despite the excellent clinical response observed in each case, objective appraisal invariably demonstrated evidence of persistent malabsorption. This was indicated by the observations that steatorrhea persisted in all patients and that flat curves of tolerance to orally taken substances and a roentgenologic deficiency pattern remained in most, even though treatment was carried out for more than a year in all but one patient and for two years or longer in some instances.

The finding of persistent malabsorption after long periods of successful gluten-free dietotherapy serves to emphasize two points, namely, (1) the possibility remains that intolerance to gluten is not the ultimate cause of nontropical sprue and (2) states of nutritional deficiency theoretically may develop unless supplemental doses of vitamins and minerals are included in the gluten-free dietary program.

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NEPHROBLASTOMA (WILMS' TUMOR)

PROGNOSIS MORE FAVORABLE IN INFANTS UNDER ONE YEAR OF AGE

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Nephroblastoma was treated in 42 children (25 girls, 17 boys) under the age of 9 years. The standard treatment, used in 26 cases, consisted of immediate nephrectomy and postoperative roentgenotherapy. The entire group of 42 patients was followed up for at least three years, and of the 20 who died postoperatively 17 died of metastases (9 the first year and 8 the second). Irradiation caused the disappearance of lung metastases in one patient but visibly retarded bone growth. Because of the ill-effects of unnecessary radiotherapy, preoperative irradiation for suspected malignant conditions of the kidneys is unsafe. The survival rate of 45% in this series of 42 patients since 1934 is gratifying by comparison with the rate of 9% found in a similar series before 1934.

Nephroblastoma (embryonal nephroma, or carcinosarcoma of the kidney), often called Wilms' tumor since the classic study by Max Wilms[1] in 1899, is one of the worst of the "organ" cancers in children. Prior to 1934, 91% of the children treated for this condition at the Babies Hospital and the Columbia-Presbyterian Medical Center died.[2] However, with modern surgery and x-ray therapy, the over-all survival rate has improved from 9 to 40% among the 42 patients treated from June, 1934, to June, 1956. Among the patients whose condition permitted operation, the survival rate has risen to 45%.

A closer look at the improved survival figures revealed that the better results were due largely to the fact that children in whom tumors were discovered before the age of 2 years showed a 70% three-year survival rate. The children in whom tumors were discovered before the age of one year had a 90% survival rate. However, in children in whom tumors were discovered after the age of 2 years, the survival rate dropped to only 18%. This tendency for a neoplasm to become more lethal as the patient grows older is quite the opposite from the usual finding in cases of cancer in adults, where the malignancies occurring in older adults usually tend to be less active than in younger adults. The more favorable response in the younger children cannot be credited entirely to the smaller size of the tumors, since all of the tumors removed were large enough to cause a palpable mass in the abdomen, and in the younger children, this mass was proportionately much larger, in relation to the size of the child, than those removed at later ages.

Neither can the greater success be attributed to greater radiosensitivity, since the tumors in all age groups tested (up to the age of 9 years) appeared to be about equal in sensitivity. Some of the very young children, early in our series, received no radiotherapy after nephrectomy and still showed an 80% survival rate. While it was evident that combinations of adverse factors, such as rupture or spillage of tumor, invasion of the renal vein, and distant metastases, all brought about a poorer prognostic outlook in general, there was still a fair number of patients who had done well despite a multiplicity of apparently unfavorable factors. Thus it became evident that we should try for a cure in every case, since some patients did unexpectedly well, for no obvious reason.

The tendency of nephroblastomas in the present study to be less lethal in younger children found no parallel in the series of 71 children with sympathicoblastomas at the Babies Hospital during the same period (1934-1956). The sympathicoblastomas studied were equally fatal among the young infants and the older children. In the infants below the age of 2 years, only 20% survived, and among the children who were from 2 to 12 years old at the time of diagnosis, only 16% were still alive.

Among the 42 patients with nephroblastoma treated since 1934, there was a slight preponderance of females over males (25 females and 17 males).[3] The tumors were equally frequent on both sides, and there were four patients with bilateral tumors. Most of these tumors occurred in children under the age of 5 years. Nine of the children were less than one year old, six from 1 to 2 years, seven from 2 to 3, eight from 3 to 4, five from 4 to 5, four from 5 to 6, one from 6 to 7, one from 7 to 8, and one from 8 to 9. The cut-off age in this series was 9 years; all of the 42 patients in this group have been followed up for three or more years since the discovery of the tumor.

From the Pediatric Urological Service of the Babies Hospital and the Squier Urological Clinic, Columbia-Presbyterian Medical Center.

Read before the Joint Meeting of the Section on Pediatrics and the Section on Urology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

All of the patients who came to operation had a large abdominal mass, easily felt by the examiner. Indeed, this was the principal complaint of most of the patients in whom the mass had been discovered by the mother, usually while washing the child. One such mass was discovered in an outpatient by a medical student while he was doing a routine examination for a draining urachus. Because the tumors were ordinarily large and globular when first detected, an intravenous urogram usually indicated marked distortion of the renal pelvis and calyces. In the case illustrated in figure 1, it was necessary to do a retrograde pyelogram, however, to differentiate nephroblastoma from adrenal sympathicoblastoma or from benign renal lesions such as cystic kidney or from hydronephrosis. Almost all of the tumors were large, with an average weight of 540 Gm. The smallest operative specimen, the one discovered by the medical student, weighed 78 Gm., whereas the largest weighed 1,850 Gm. At autopsy, one tiny unsuspected tumor weighing only 3 Gm. (1 cm. in diameter) was found, but the heaviest weighed 3,000 Gm. The patient with the 1-cm. tumor had died of progressive subcortical encephalopathy (Schilder's disease).

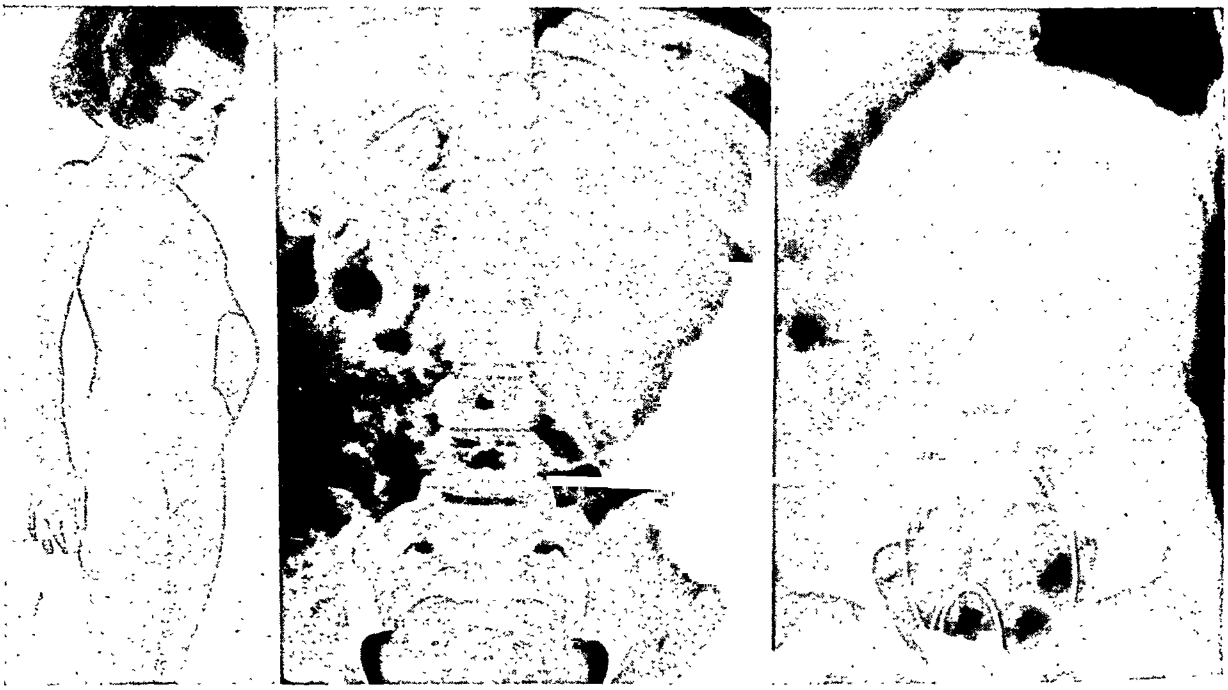

Fig. 1.—Rapidly growing nephroblastoma in 5-year-old girl. *Left,* abdominal mass easily seen. *Center,* intravenous pyelogram showing enlarged left kidney. *Right,* retrograde pyelogram taken five weeks after intravenous pyelogram shows that mass has grown considerably, is displacing stomach upward and medially, and has compressed and distorted all calyces. Despite removal of tumor and vigorous radiotherapy, child died within 14 months.

Results of Therapy

Different methods were used in treating the 42 patients (table 1). Among those who received preoperative radiotherapy followed by nephrectomy, the results were poor. While some of the tumors decreased markedly in size because of the preoperative radiotherapy, viable neoplastic cells were found, which were still continuing to divide, in the irradiated tumors at the time of their removal. Furthermore, we have observed in the children treated between 1934 and 1940 that a number received vigorous radiotherapy to kidney masses which at operation were found not to be tumors. Any unnecessary radiation is seriously traumatic to a child.

The largest group (26 patients) underwent immediate nephrectomy followed by postoperative radiation with the 500-kv. machine, and in only one case was the 24-million volt betatron used. Nephrectomy, followed by radiotherapy, is our standard treatment regimen at this time, and its effectiveness is demonstrated by the 42% of survivals in this group. Surprisingly, the five patients who underwent nephrectomy only have done well, with four of the five still alive. The entire group of 42 patients has been followed up for at least three years at this writing.

Radiotherapy has been effective in causing the disappearance of occasional lung metastases, such as one discovered six months after nephrectomy in a 9-month-old boy. This child is now 7 years old and well. However, radiotherapy is not without ill-effects on the body of the patient. We have seen several children whose bones have been stunted on one side by the radiotherapy and one patient whose ovary was completely atrophied on one side due to the treatments. It is desirable to irradiate both sides of the spine in order to prevent asymmetrical growth and development of the bodies of the vertebrae.

Of the 20 patients who died postoperatively, 17 (85%) died of metastases within the first two years (9 the first year and 8 the second) after nephrectomy. There were no operative deaths. One patient died *in the third year and one in the fourth year* after operation. In one who died after the 10th year no tumor was found. This led to the conclusion that if a patient survives two years after nephrectomy there is a fair chance that he may be cured, despite *the fact that occasionally cases* of recurrence are reported many years later. Other authors[4] have made similar observations.

TABLE 1.—*Methods of Treatment and Survival Rates*

Methods of Treatment	Patients, No. Total	Alive	Dead
No treatment	5	...	5
Radiotherapy only	1	...	1
Combined treatment			
Preoperative radiotherapy and nephrectomy	1	1	...
Nephrectomy and postoperative radiotherapy	26	11	15
Preoperative radiotherapy, nephrectomy, and postoperative radiotherapy	4	...	4
Nephrectomy only	5	4	1
Total	42	16	26

It was not surprising to find that the patients with kidney tumors in the lower pole showed most successful results, presumably because the tumors were more easily palpable and were surrounded by fatty coverings which could absorb some local extension and still be removed successfully with the tumor. On the other hand, tumors of the upper pole were not so easily palpated, were not padded by surrounding fat, and were so close to the diaphragm and great vessels that invasion of these organs was frequent, with attendant poor survival. The patients in whom tumors were encapsulated did well, whereas those in whom capsules were penetrated or broken at operation did poorly. The patients in whom tumors invaded the renal vein also did poorly, as might be expected.

Signs and Symptoms

All of the tumors observed produced a palpable abdominal mass. In two patients "without complaints" the kidney tumors were discovered incidentally—one during physical examination for urachal discharge and the other as the result of a routine roentgenogram of the chest. Many had a high sedimentation rate, which turned out to be a bad prognostic point. Hypertension in association with nephroblastoma has been previously reported,[5] and in this series 60% of those children who were tested had hypertension. A surprisingly large percentage (25%) had either gross hematuria or erythrocytes in the urine, findings which have not been emphasized in the many publications concerning this tumor.

Temperatures ranging from 100 F (37.8 C) (rectal) were present in 44% of the patients. There was no apparent relationship between the height of the temperature and the size of the tumor. Pronounced leukocytosis was found in the children who had hyperpyrexia, and fever was often present in children who had been vomiting and were dehydrated or who had metastases or extensive necrosis within the tumor. It would appear that the presence of unexplained fever should make one suspect the presence of nephroblastoma.

The interval between the first symptoms and the time of operation did not appear to affect the prognosis as long as the interval was less than three months.

Anemia, with hemoglobin values ranging from 7.5 to 10.9 Gm. per 100 cc. and red blood cell counts ranging from 3,040,000 to 3,860,000 per cubic millimeter were present in 25 of 40 cases in which these findings were recorded. Anemia was more frequent in the children with fairly large tumors.

Pathology

Most of the tumors, when their weights were compared with the body weight, were found to be considerably larger than kidney tumors in adults. The smallest tumor weighed 78 Gm., the largest surgical specimen weighed 1,850 Gm., and the heaviest specimen found at autopsy weighed 3,000 Gm. The average weight was 540 Gm. The upper pole, lower pole, or middle segment of the kidney were found to be the seat of the tumor with about equal frequency (table 2); but of 14 patients whose tumor involved the upper pole, 10 died, while only 3 died of the 8 whose tumors were in the lower pole. Of 16 patients whose tumors were well encapsulated, 12 (74%) are alive. A tumor in a horseshoe kidney[6] and another in an innocent appearing multilocular cyst of the kidney[7] were encountered. A 4-day-old infant in this series is among the youngest patients reported[8] to date to undergo nephrectomy for nephroblastoma (fig. 2).

TABLE 2.—*Area of Kidney Involved by Tumor, as Noted in Surgical and Autopsy Specimens*

Area	Patients Total, No.	Alive, No.	Dead No.	%
Entire kidney	4	1	3	75
Upper pole	14	4	10	71
Middle segment	14	6	8	57
Lower pole	8	5	3	37
Not stated	2	0	2	100
Total	42	16	26	...

The histological picture in patients with nephroblastoma has been as follows: pattern predominantly carcinoma in 20 tumors, carcinosarcoma in 18, and sarcoma in 3, and in 1 instance the microscopic picture was unknown. Although there was no significant relationship between the histological appearance of the tumor and survival, three patients with sarcoma were cured of the disease. (One of these children died 10 years after nephrectomy from renal failure due to hydronephrosis caused by a congenital ureteropelvic stricture, but showed no evidence of residual or metastatic nephroblastoma.)

Differential Diagnosis

In the study of relative frequency of the various lesions which cause abdominal masses in children, over 6,000 hospital records were carefully reviewed, with the findings shown in figure 3. Of the 653 children with palpable abdominal masses,[9] slightly more than half of the masses were due to "medical conditions" such as hepatosplenomegaly and leukemia. In 281 patients with masses, operation was performed; in about half there was involvement of the urinary tract, particularly the kidneys. In the other half the mass developed from retroperitoneal or intraperitoneal structures other than the urinary tract. Hydronephrosis and cystic renal disease each produced as many abdominal masses as did nephroblastoma. Of the extraurinary lesions which at times resembled nephroblastoma, those frequently encountered were sympathicoblastoma, lymphosarcoma, and teratoma.

In a study of the sympathicoblastomas, only those which arose from the adrenal glands or the pararenal sympathetic ganglions resembled nephroblastoma in the roentgenograms. In about 80% of the 72 patients with sympathicoblastoma registered at the Babies Hospital during the same period, the tumors had developed in the adrenal gland or in the pararenal sympathetic ganglions. Sympathicoblastomas, thus, frequently resembled nephroblastoma and displaced the kidney or distorted it sufficiently that retrograde pyelograms were necessary to differentiate the two types of malignancy. The sympathicoblastomas tended to metastasize to bone, whereas the nephroblastomas did not. When a patient with an abdominal mass also showed an obvious metastasis in a frontal bone, in the orbit, or in one of the long bones, the diagnosis was almost always sympathicoblastoma. If the mass grew rapidly and extended across the midline, becoming nodular and fixed, it was more often sympathicoblastoma than nephroblastoma. Most of the nephroblastomas confined themselves to one side of the abdomen and were globular and somewhat mobile.

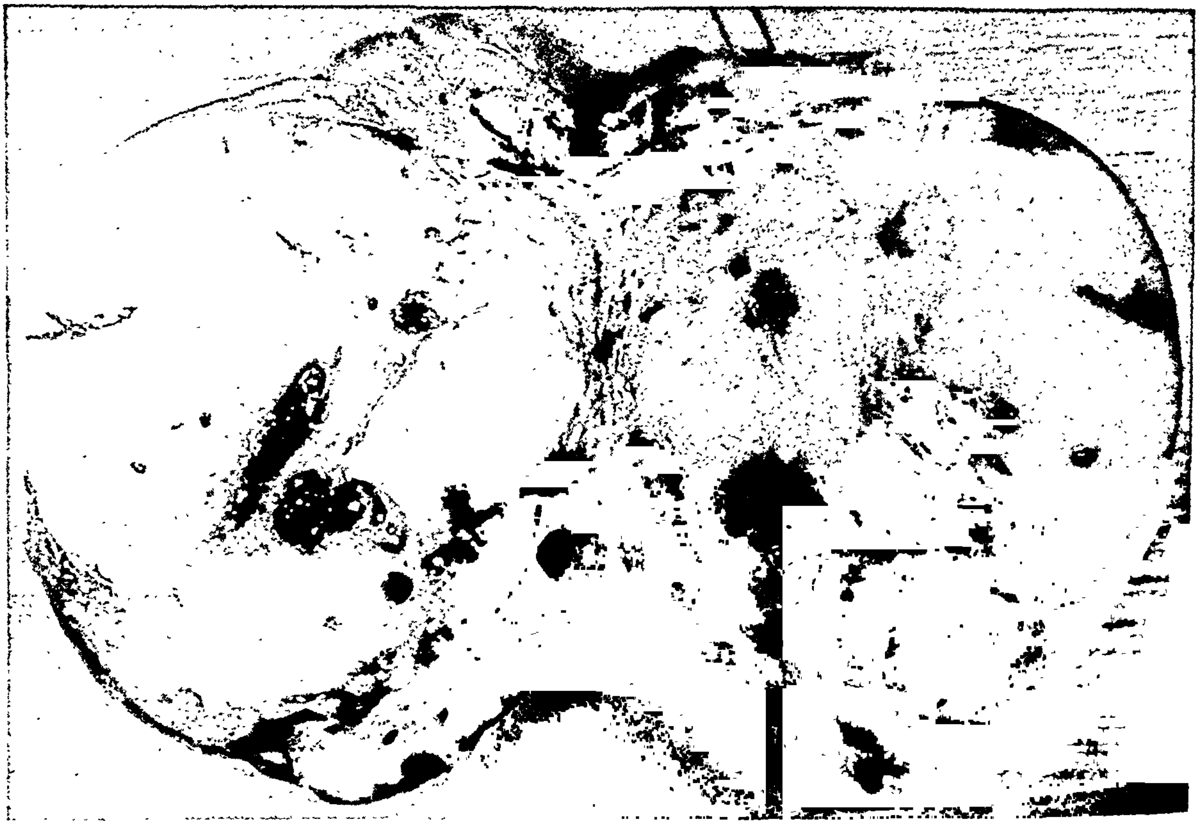

Fig. 2.—Nephroblastoma discovered at birth and removed when baby was 4 days old. Note large size of tumor. Patient was well three years after excision of tumor and postoperative radiotherapy.

Sympathicoblastomas frequently ...cially[5] for the calcifications in their substance (30%), ...fections of 2 (5%) of our series of 42 nephroblastomas any calcium. Of these two, the calcium appea... edi- one after radiotherapy, and the other was t... largest tumor in the series.

Hydronephrosis was the most common single cause in 285 patients with palpable "surgical" abdominal masses. Masses due to hydronephrosis frequently could be transilluminated if the patient was taken into a dark room and a strong light applied behind the mass. Retrograde pyelograms almost always revealed the diagnosis in advance. Another cause for an expanding mass in the upper pole of the kidney was a double renal pelvis, one-half of which was obstructed. We saw many ureteroceles at the lower end of a double ureter, which was obstructed, one of the ureters causing the corresponding pole of the kidney to expand in a manner suggesting tumor. These cases were easily cured by heminephrectomy, after cystoscopic examination provided the accurate diagnosis.

Increase in the size of the kidneys may be caused by cystic disease, infiltration with lymphosarcoma, or infiltration with amyloidosis. Cystic diseases of the kidneys were found in about 30 patients of the 285 with palpable abdominal surgical masses; half of these were serous cysts (multicystic, polycystic, multiple cysts, multilocular cystic kidney, and solitary cyst of kidney). Pheochromocytoma, of which we have seen four cases in children, rarely grew large enough to cause an abdominal mass in this age group, although some of the 52 pheochromocytomas in adults weighed more than 300 Gm. (One weighed 1,000 Gm.)

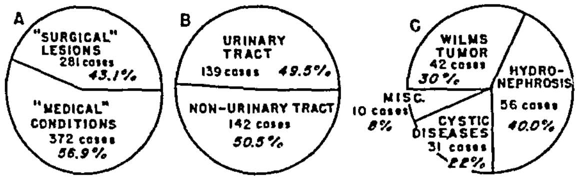

Fig. 3.—Frequency of palpable masses in 653 infants and children. *A*, all masses; *B*, all "surgical" masses; and, *C*, genitourinary masses only. Kidney was found to be commonest source of "surgical" masses.

Benign lesions causing enlargement of the kidney occur so frequently that they must be differentiated from malignant lesions before vigorous measures such as radiotherapy are applied. This is one of the strong arguments against preoperative radiotherapy for suspected malignant conditions of the kidneys. We have seen several children who suffered the ill-effects of radiation therapy unnecessarily, under these circumstances.

Summary

This study revealed that the age of the patient at the time of nephrectomy was the most important single factor in determining prognosis. Of the chil-

Skin.—Lesions involving the skin respond uniformly to griseofulvin therapy. (Dermatitis of the thicker skin of the hands and feet is discussed separately below.) Symptomatic relief of pruritus can be promised in 48 to 96 hours. The first visible

TABLE 1.—*Data on 311 Sites of Involvement in 200 Patients Studied, Treated, and Followed up to May, 1959*

canis	10
douini	23
urans	1
inl	1
	2
	2

Nails	
Trichophyton rubrum	52
Trichophyton mentagrophytes	3
Trichophyton violaceum	1
Epidermophyton floccosum	1
Trichophyton schoenleini	1
Potassium hydroxide test, positive result	18
Total	76
and extremities	
hyton rubrum	65
um audouini	5
canis	6
	1
osum	1
i	1

bla... vival r... June, 1934, Thirty-six of ... tomy; of these, 1... the study (five from ... years, and the remainin...

Of the children who died ... nephroblastoma, 85% died with... after operation. There were no in... erative deaths. Of the 42 recent patie... females and 17 males. Their ages range... days to 9 years.

Abdominal mass was the presenting complaint[14] ... 60% of the cases, but a mass was palpable in every patient. Vomiting, abdominal pain, fever, and hematuria occurred in some of the children. Five patients had gross hematuria. Hypertension was found in 60% of the patients in whom the blood pressure was recorded. None of 11 children with a high sedimentation rate (35 to 90 mm. in one hour) survived.

Intravenous urography often sufficed in confirming the clinical impression of nephroblastoma, but retrograde pyelography was the more reliable procedure. Preoperative radiotherapy proved to be an unsatisfactory procedure in the four cases in which the full course was given. Furthermore, intensive preoperative radiotherapy was given in some instances to kidneys which later were found to contain benign lesions. Preoperative and/or postoperative radiotherapy proved at times to be traumatic to the vertebrae, iliac bones, and ovaries. Prompt nephrectomy, followed by immediate postoperative radiotherapy, produced better results.

Accurate differential diagnosis between nephroblastoma and other abdominal masses should be possible in practically all cases, provided an adequate study and interpretation are made of the clinical history, physical examination, and laboratory and roentgenographic findings. Any child with fever of unknown origin, hypertension, pyuria, hematuria, or other urinary symptoms, with or without an abdominal mass, should have a thorough urologic investigation. Early diagnosis, coupled with prompt and adequate treatment, should bring about a great increase in the number of children with a favorable prognosis.

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The late Dr. G. F. Cahill, Drs. G. W. Fish, C. T. Hazzard, J. N. Robinson, R. Yeaw, R. Seidel, T. J. Sullivan, and other members of the Squier Urological Clinic gave permission for the inclusion of their private patients in this review.

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GRISEOFULVIN FOR THE SYSTEMIC TREATMENT OF DERMATOMYCOSES

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Griseofulvin, an antibiotic obtainable from at least four kinds of Penicillium, has been found effective in certain experimental fungous infections of animals as well as in fungous diseases of man. It was used in 200 patients with superficial fungous infections at 311 sites of major involvement. The organism most frequently found was Trichophyton rubrum, identified in 185 sites. The dosage of griseofulvin varied from 0.5 to 1.0 Gm. by mouth. One gram per day is recommended. When the lesions did not involve the nails, palms, or soles, three weeks of therapy usually was adequate. Even with lesions of the palms and soles, relief from itching occurred in two to six days; vesicles and scales disappeared and cultures usually became negative in two to six weeks. It was necessary to keep in mind the fact that nails grow slowly and that the fungous infection may be superposed on other disease. Until more experience with this drug accumulates, monthly blood counts are advised, but in this series no significant manifestations of toxicity were noted.

For the first time an orally administered drug, griseofulvin, has been effective in curing superficial fungous infections of the skin (ringworm), nails, and hair. Nearly 20 years passed from the time of the first report of its isolation in 1939 by Oxford and associates[1] and its administration to human beings with superficial mycotic disease. The drug, supplied by Glaxo Laboratories of England, was first given to patients in the fall of 1958, apparently very nearly simultaneously by three independent groups—Riehl[2] in Vienna, Williams and associates[3] in London, and ourselves[4] in Miami. The present paper is a report of our further experience with 200 patients who have been treated for various fungous infections and observed sufficiently long for conclusions to be drawn.

The antibiotic was initially isolated from Penicillium griseofulvum[1] but also has been isolated from P. patulum, P. janczewskii, and P. raistrickii.[5] A "curling factor" which produced short, stunted germ tubes of Botrytis allii was isolated in 1946 by Brian and associates[6] from cultures of P. janczewskii. Subsequently, the curling factor was found to be identical with griseofulvin, and its chemical structure was established by Grove and his col-

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leagues.[7] The drug was used commercially[5] for the prevention and treatment of Botrytis infections of lettuce and Alternaria blight of tomatoes.

The possible usefulness of griseofulvin in medicine for human beings was not appreciated until Gentles[8] reported its effectiveness in experimental infections with Microsporum canis and Trichophyton mentagrophytes in guinea pigs. Martin[9] has indicated that he too had worked along similar lines. The drug has also been used successfully to treat Trichophyton verrucosum infections in cattle.[10]

In our first report,[4] 31 persons infected with a variety of fungi in the genera Trichophyton, Microsporum, and Epidermophyton involving skin, hair, and nails showed uniform improvement after therapy with orally given griseofulvin. Patients treated by Williams and associates[3] and Riehl[2] have also shown regular improvement. Topical use of griseofulvin, however, was surprisingly ineffective in a study by Peterkin.[11]

Griseofulvin is a white, bitter, neutral, thermostable compound with the chemical name 7-chloro-2′,4,6-trimethoxy-6′-methyl spiro [benzofuran-2(3H), 1′-[2]cyclohexene]-3,4′-dione. The structural formula is shown in figure 1.

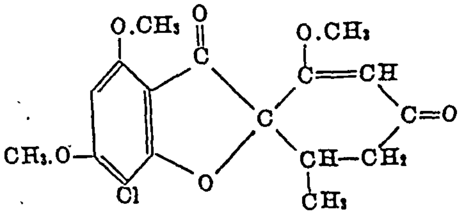

Fig. 1.—Structural formula of griseofulvin.

It is poorly soluble in water but slightly soluble in methanol and ethanol. It withstands autoclaving at 122 C (250 F) for 30 minutes) at a pH of 7 without loss of potency and is stable in the dry form for at least 20 months at 37.8 C (100 F).

All of the dermatophytic fungi (Microsporum, Epidermophyton, and Trichophyton) are inhibited by less than 0.4 μg. of griseofulvin per milliliter.[12] Candida albicans, the deep systemic fungi, and bacteria seem insensitive even to 30 μg. per milliliter.

Clinical Results

The present study of 200 cases of superficial fungous infection with 311 sites of major involvement of the body (table 1) confirmed our earlier favorable observations.[4] Because response to therapy depends on the rate of keratinization and the time necessary for desquamation of infected keratinized structures, it is more convenient to discuss responses to griseofulvin by major site of involvement than according to the organism. In general, species of Trichophyton, Epidermophyton, and Microsporum have responded in like manner to similar doses of griseofulvin.

Skin.—Lesions involving the skin respond uniformly to griseofulvin therapy. (Dermatitis of the thicker skin of the hands and feet is discussed separately below.) Symptomatic relief of pruritus can be promised in 48 to 96 hours. The first visible change is a decrease in erythema and induration followed by a slower involution of scaling and hyperpigmentation in several weeks (fig. 2). Without any local treatment, lesions of nonintertriginous areas are usually completely gone in two to four weeks, except for long-lasting pigmentation in Negroes or other persons with dark skin (fig. 3). If a concomitant bacterial or monilial infection is present in intertriginous areas, dermatitis sometimes persists after the infection with the dermatophyte has cleared. Specific local antibacterial or antimonilial therapy may be necessary. Erythrasma and pityriasis versicolor do not respond to treatment with griseofulvin.

TABLE 1.—*Data on 311 Sites of Involvement in 200 Patients Studied, Treated, and Followed up to May, 1959*

Scalp	
Microsporum canis	10
Microsporum audouini	23
Trichophyton tonsurans	1
Trichophyton schoenleini	1
Trichophyton rubrum	2
Potassium hydroxide test, positive results	2
Total	39
Hands and feet	
Trichophyton rubrum	66
Trichophyton mentagrophytes	12
Trichophyton violaceum	1
Epidermophyton floccosum	2
Potassium hydroxide test, positive result	22
Total	103
Nails	
Trichophyton rubrum	52
Trichophyton mentagrophytes	3
Trichophyton violaceum	1
Epidermophyton floccosum	1
Trichophyton schoenleini	1
Potassium hydroxide test, positive result	18
Total	76
Trunk and extremities	
Trichophyton rubrum	65
Microsporum audouini	5
Microsporum canis	6
Trichophyton mentagrophytes	1
Epidermophyton floccosum	1
Trichophyton schoenleini	1
Potassium hydroxide test, positive result	14
Total	93

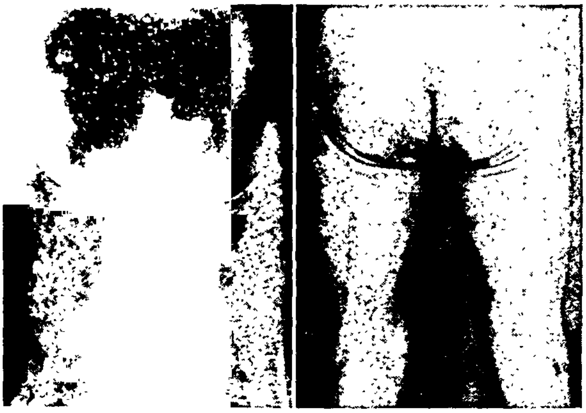

Fig. 2.—*Left,* tinea corporis of five years' duration, caused by Trichophyton rubrum. *Right,* result after three weeks of therapy with griseofulvin, 1.0 Gm. orally per day.

Repeated direct examinations of scrapings in potassium hydroxide and cultures at 72-hour intervals have also confirmed the earlier observation that cultures usually show negative results in one to two weeks and examinations with use of potassium hydroxide show negative results after about two weeks of therapy.

After initial clearing of skin lesions six patients have subsequently had relapses in periods of three weeks to several months after treatment was stopped. Five of the six patients had nail involvement, the importance of which was not appreciated at the time the patients were originally treated. It is now thought that, if the nails are involved, treatment should be continued until the nails are normal, to obviate cutaneous relapse.

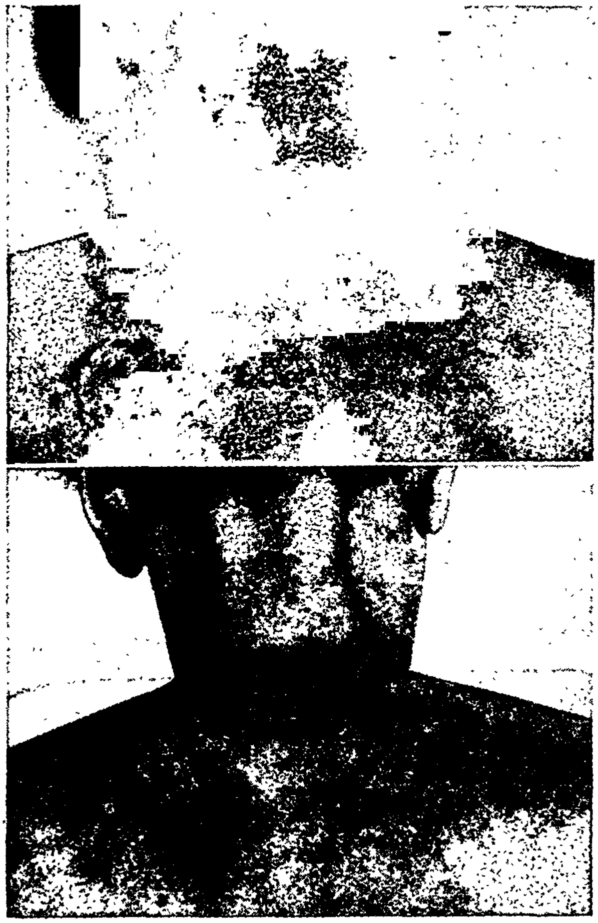

Fig. 3.—*Above,* tinea corporis of two years' duration, caused by Trichophyton rubrum, in a Negro. *Below,* result after one month of therapy with griseofulvin, 1.0 Gm. orally per day.

The dosage of griseofulvin for adults has in our more recent experience varied between 0.5 and 1.0 Gm. per day. Patients with Trichophyton rubrum will respond to 0.5 Gm.; however, in some persons the lesions do not seem to clear completely until 0.75 or 1.0 Gm. per day is administered. No patient unresponsive to 1.0 Gm. per day has been observed. When lesions involve only the skin and not nails, palms, or soles, about three weeks of therapy usually is adequate.

Palms and Soles.—Lesions of the palms and soles clear more slowly than lesions of skin elsewhere because of the greater thickness of the stratum corneum in these areas. Symptomatic improvement of itching occurs in two to six days. Within two to six weeks complete disappearance of vesicles and scaling can be anticipated (fig. 4). Cultures usually become negative in two to six weeks, with a disappearance of the organism in potassium hydroxide after two to six weeks. Two unusual cases have been seen in which the skin returned to normal but the fungi persisted for a number of weeks. Further studies of these patients are in progress.

Lesions of the feet and hands especially require skilled, accurate diagnosis. Patients who have nonmycotic eczematous eruptions or moniliasis will not respond to griseofulvin treatment. In addition, there are a few patients who have a fungous infection superimposed on an eczematous eruption. Even though results of potassium-hydroxide examination and cultures become negative in such patients, complete clearing requires additional local treatment directed at the eczematous eruption. If moniliasis coexists, it also may prevent healing and require appropriate topical therapy in addition to oral use of griseofulvin for the dermatophytosis. As in other areas of the skin, relapse after cessation of treatment may occur on the palms or soles in the presence of nail involvement.

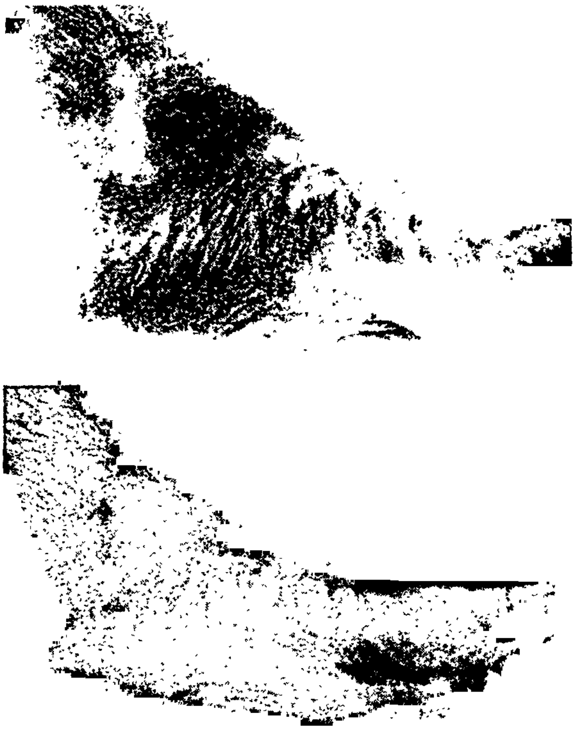

Fig. 4.—*Above,* dermatophytosis of 15 years' duration, caused by Trichophyton rubrum. *Below,* result after six weeks of therapy with griseofulvin, 1.0 Gm. orally per day.

The recommended dose of griseofulvin for treatment of lesions of the feet and hands is 1.0 Gm. a day. Response is seen with 0.5 or 0.75 Gm., but it is slower and may not be complete. Treatment should be given for four to eight weeks.

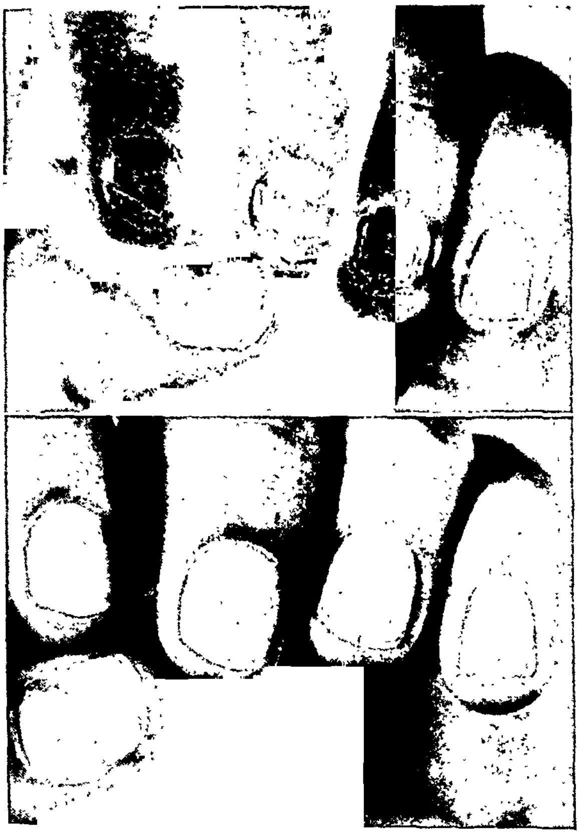

Fig. 5.—*Above*, onychomycosis of fingernails of eight years' duration, caused by Trichophyton rubrum. *Below*, results after four months of therapy with griseofulvin, 0.5 Gm. orally per day.

Nails.—Because of the slow rate of nail growth, several weeks must elapse before clinical improvement is first noted at the proximal end of the nail. The distal mutilated nail plate may undergo very little change as it slowly moves out. Fingernails grow out completely in about four months (fig. 5), and toenails take six months or more (fig. 6). At the present time, continuous treatment of the nails is recommended to prevent a relapse of lesions of nails or skin. We have followed up one patient who received only six weeks' treatment, during which time his four infected nails improved. Four months later two of the nails showed complete cure but two others showed relapse. A dose of 1.0 Gm. per day seems sufficient for most nail infections.

As for eruptions of the feet, careful mycologic study of the nails is essential. Psoriasis of the nails, for example, is sometimes difficult to differentiate from onychomycosis. Pure Candida albicans (monilial) infections do not respond to griseofulvin therapy. In at least one instance of a mixed infection with C. albicans and Trichophyton violaceum, improvement has occurred with combined local treatment with nystatin cream and systemically administered griseofulvin. Bacterial infection may also occur, especially with Pseudomonas aeruginosa, with development of discoloration of the nail. Embarrassment of the physician and false hopes of the patient will be prevented by establishment of an accurate diagnosis before the six-month course of treatment is begun.

Hair and Scalp.—All of our patients treated to date (table 1), having either an endothrix or ectothrix fungous infection of the scalp, have showed clearing of the infection after oral use of griseofulvin. As shown by Wood's light, three weeks of treatment with 0.5 to 1.0 Gm. a day seems sufficient for patients who have Microsporum infections. Several children have shown clearing after single orally given doses of 5 Gm. and even 3 Gm. (fig. 7). This may be of value in controlling epidemics among children unlikely to get regular daily medication. Two or three weeks after the beginning of oral therapy, clipping of the hair is usually advised to remove the distal infected part of the hair. The sustained good response observed in several girls without clipping indicates that the actual need for clipping has not been proved. The demonstration[13] that griseofulvin is deposited in the hair may explain these results.

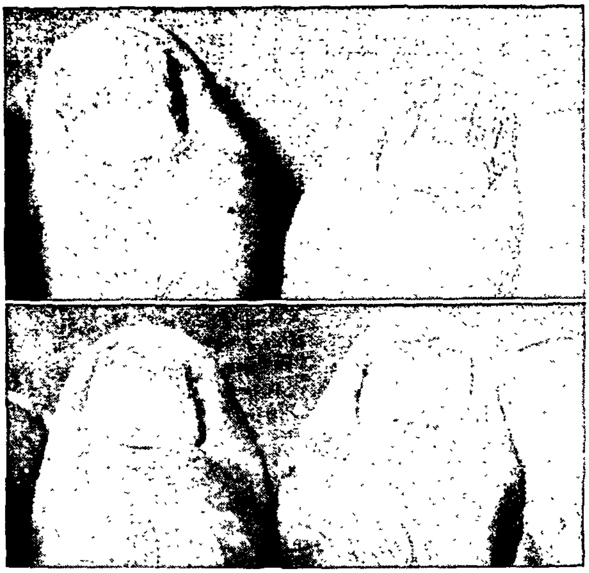

Fig. 6.—*Above*, onychomycosis of great toenails of six years' duration, caused by Trichophyton rubrum. *Below*, results after six months of therapy with griseofulvin, 1.0 Gm. a day.

Although we have treated only a few patients with Trichophyton infections of the scalp, they have shown favorable response. The patient with a Trichophyton tonsurans infection of 60 years' duration reported cured in our initial report has now remained cured with no further treatment after six months of observation. Trichophyton (nonfluorescent ringworm) infections of the scalp probably should be treated with 1.0 Gm. a day for four to eight weeks.

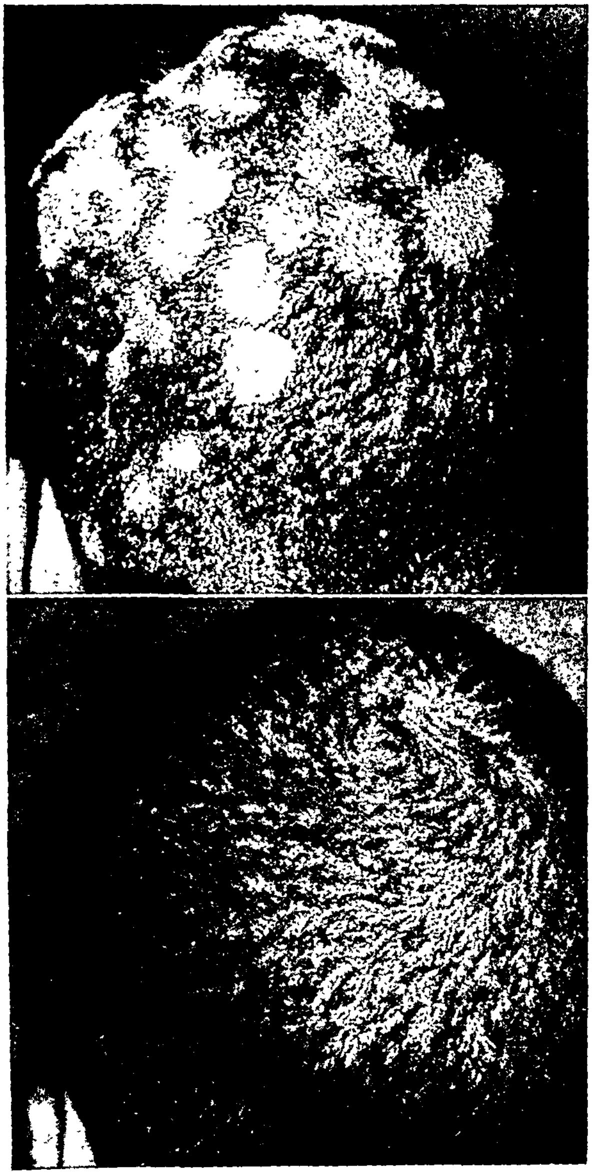

Fig. 7.—*Above*, tinea capitis of four months' duration, caused by Microsporum audouini, in a 6-year-old Negro boy. *Below*, results seven weeks after single dose of 5 Gm. of griseofulvin.

Toxicity

No significant toxic manifestations of administration of griseofulvin have been noted in our series of 200 patients. Symptoms which have been reported by patients and thought to be caused by the drug include mild gastrointestinal distress or loose stools and headaches. These have appeared in a minority and disappeared with continued administration of griseofulvin. Two patients developed urticaria after several weeks of therapy. The urticaria disappeared when the therapy was stopped and was reproduced by further administration of griseofulvin. Cross-sensitivity with penicillin has not been noted.

As reported in our earlier series, no abnormalities of liver function, kidney function, or blood chemistry have been found.[4] The marrow and peripheral blood counts have shown no deviations attributable to griseofulvin. In table 2 the results of 212 blood counts are reported to indicate the lack of significant toxic depression in our patients. We continue to advise monthly blood counts for patients on long-term therapy, however, because experience with the drug is still relatively limited.

Table 2.—*Average Peripheral Blood Counts of Patients Treated with Griseofulvin*

	Counts Performed, No.	Hemoglobin Level, Gm. %	Hematocrit Value	White Blood Cell Count, per Cu. Mm.	Lymphocytes, %	Polymorphonuclear Leukocytes, %	Eosinophils, %	Monocytes, %	Basophils, %	Platelets, per Cu. Mm.
Children Under 12 Years of Age										
Before treatment	10	10.9	39.1	8,815	50	42	6	1	1	295,000
During and after treatment	21	11.2	36.6	7,760	48	43	5	3	1	306,000
Children Under 12 Years of Age Given Single Large Dose										
Before treatment	7	12.0	37.5	7,940	51	41	4	2	2	258,000
After treatment	24	11.1	36	7,329	47	44	6	2	1	322,000
Patients Over 12 Years of Age										
Before treatment	48	13.1	42	7,931	34	57	4	4	1	261,000
During and after treatment	102	12.6	41.4	7,950	34	58	4	3	1	250,000

Because griseofulvin given to animals in doses in excess of 50 times that used in man inhibits cell division in a manner similar to that resulting from use of colchicine,[14] studies of blood cell formation and spermatogenesis have been of particular interest. Multiple sperm counts have been determined on 15 patients in our series. None of them has shown significant depression, even though some of the patients had been taking 1.0 Gm. of griseofulvin per day for as long as six months. In five men a series of sperm counts was done before drug therapy was started, and counts were then done at about weekly intervals; these were the most meaningful data obtained. The results show no drug-induced depression of spermatogenesis in patients after four months of treatment. This study is being continued.

Comment

The mechanism of action of griseofulvin is as yet obscure. There seems no doubt that, when ingested, the drug is absorbed and deposited in the keratinized structures of the stratum corneum, hair, and nails. It apparently differs from normal serum antifungal factors[15] in its ability to penetrate the epidermal barrier from below. Because it is fungistatic rather than fungicidal, long-term therapy is required to insure removal of all infected structures. In studies being reported elsewhere[12a] it has been shown that fungi can be immersed for weeks in mediums containing griseofulvin, and, even though there is no growth during this period, when the mycelia are removed and washed they grow out readily. It was also of interest to note that the drug seems to have no effect on oxidative metabolism of the fungus as measured in the Warburg apparatus.[12a] We have been unable to produce drug resistance in T. rubrum by growing it in minimal amounts of griseofulvin-containing medium, nor have we encountered clinical resistance.

In the rare instances when relapse occurred in our patients, it was of interest to note that it was usually at the precise sites of previous ringworm. In most instances we had satisfied ourselves that there was no detectable fungus left on the skin as determined by repeated scrapings and culture. Nonetheless, when cutaneous relapse occurred in patients with inadequately treated onychomycosis and the fungus apparently was spread from the nails, it often did not pick new sites but caused reappearance of the old ringworm. This may be of some general significance and may indicate that such localized areas of skin are particularly susceptible to infection. If this is true, it may be expected that exogenous sources of the ubiquitous dermatophytes will be the source of future "relapses" in such patients. To date relapse or reinfection has been negligible, but in the few cases seen re-treatment with griseofulvin was as quickly effective as originally.

Although most cases of dermatophytosis have cleared clinically and as indicated by culture after four to six weeks, we have noted two patients in whom fungi persisted on the feet even though complete clinical clearing occurred. Of course it is well known that dermatophytes can be isolated from time to time from perfectly normal feet, but the importance of persistent fungi in clinically cured patients has not yet been determined.

Summary

Two hundred patients with proved cases of superficial fungous infections have been treated with a new orally administered antibiotic, griseofulvin. Dermatomycoses of the skin, nails, and hair can almost invariably be cleared with use of this drug. Griseofulvin appears to be of low toxicity for man. No specific contraindications to it are known. Periodic blood counts should be taken during prolonged therapy. A dose of 1.0 Gm. per day is recommended until clinical clearing has occurred—about three weeks for skin lesions, four to six weeks for foot and hand lesions, three weeks for Microsporum infections of the scalp, six weeks for nonfluorescent infections of the scalp, four months for lesions of fingernails, and six months for lesions of toenails. Mycologic and bacteriological studies are desirable for accurate diagnosis and follow-up.

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TOXICOLOGICAL STUDIES AND EFFECTIVENESS OF GRISEOFULVIN IN DERMATOMYCOSIS

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Griseofulvin was used to treat ringworm infection in 32 patients. In addition to observations on its effectiveness, close watch was kept for possible side-effects, and laboratory tests were applied to detect signs of damage to kidneys, testes, liver, brain, and hematopoietic tissues. Dosages usually were 0.5 or 1.0 Gm. of griseofulvin per day by mouth, and the treatment generally continued for 30 days. The organism most frequently found (12 cases) was Trichophyton tonsurans. Striking success was the rule, with the disappearance of fluorescent hairs and resumption of normal growth in previously deformed fingernails. The only indication of adverse effects was an increase in the proportion of mature lymphocytes found in the differential count. Under the conditions of this study griseofulvin appeared to be an effective and safe antibiotic for use in treating superficial fungus infections.

In December of 1958 a new chapter was written in the "pageant of healing." At the Academy of Dermatology, Dr. Harvey Blank[2] announced his preliminary findings with a new antibiotic, griseofulvin (Grifulvin, Fulvicin). With the exception of the dubious effect of iodides as internal medicaments for superficial fungus infections in humans, little else than topical formulas were theretofore available. Gentles' report[3] showing the effect of griseofulvin on superficial mycoses in guinea pigs made inevitable the trial of the drug in man.

Griseofulvin was isolated, oddly enough, in 1939 by Oxford and associates,[4] the same year that Fleming discovered the antibiotic effect of penicillin. So, now, the "source of confusion to the beginner and of annoyance to the more experienced,"[5] the bane and curse of earlier bacteriologists and mycologists, the contaminant, Penicillium, the source of griseofulvin, emerged in 1959 as a still further boon to man. Of course, unheralded and unrecognized, this lowly mold has worked for man all along. Another interesting fact to ponder is that, like the sulfonamides and penicillin, griseofulvin was known many years before its value to man himself was appreciated. One wonders if perhaps a cure for cancer, tuberculosis, diabetes, or mental illness is not now on the chemist's shelf.

This report concerns the use of griseofulvin in the control of ringworm infection of 28 children at the Austin State School (for the mentally retarded) and 4 private patients. All cases, except as noted in the table, were of either tinea capitis or mixed tinea capitis and tinea corporis. Three patients (cases 27, 29, and 30) had involvement of the nails only. Our results seem to support Blank's impression that griseofulvin is extremely effective in the treatment of certain superficial fungus infections and safe in therapeutic doses.

Although no geographical area in the United States seems to be immune to troublesome fungus infections, states bordering Mexico suffer near epidemics at times. In Texas this factor, plus the warmer climes, results in fungus infections accounting for an appreciable part of clinic and private practice. Particularly troublesome within recent years has been a noticeable increase of Trichophyton tonsurans scalp infections. In southern climes, at least, many of these infections have been nigh incurable. Nearly every practicing dermatologist has had patients with tinea corporis or onychomycosis caused by Trichophyton rubrum, e. g., who have been affected for years, with little or no response to the most vigorous local therapy. Most cases of tinea capitis, regardless of the causative organism, last for two to four months, with many cases seemingly incurable short of x-ray epilation—and even this modality is not always certain to cure the patient. The psychological trauma of such prolonged treatment is serious, especially in a child, requiring, as it does in tinea capitis, cutting the hair, manual epilation, and wearing stocking caps to (and in) school.

Griseofulvin is a fermentation product of three species of Penicillium: P. patulum, P. griseofulvin, and P. janczewski.[5] Its structural formula is shown in figure 1. The "curling factor," an antibiotic derived from P. janczewski by Brian and co-workers[6] in 1946, was shown by Grove and McGowan[7] to be identical to griseofulvin. Paget and Walpole[8] have noted certain cytological effects of griseofulvin. They state that the median lethal dose of the drug given to rats intravenously is about 400 mg.

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Type of Dermatophytosis and Results of Therapy with Griseofulvin in Thirty-two Patients

Case No.	Sex	Concomitant Disease	Age, Yr.	Direct Microscopic Examination	Type of Fungus	Duration of Infection, Mo.	Site of Infection	Daily Dose, Gm.	Duration of Medication, Days	Direct Microscopic Examination on 28th Day	Cultures Taken on 28th Day	Final Result
1	M	Congenital cerebral maldevelopment, nonspecific	11	Positive	M. audouini	8	Scalp	1	42	Negative	Negative	Recovered
2	F	Congenital cerebral maldevelopment with cerebral palsy	6	Positive	T. tonsurans	4	Scalp	1 0.5	30 12	Negative	Negative	Recovered
3	M	Congenital cerebral maldevelopment due to familial factors	9	Positive	M. audouini	8	Scalp	1 0.75	30 12	Negative	Negative	Recovered
4	M	Congenital cerebral maldevelopment, nonspecific	9	Positive	T. tonsurans	6	Scalp	1 0.5	30 12	Negative	Negative	Recovered
5	M	Congenital cerebral maldevelopment with cerebral palsy	10	Positive	T. tonsurans	8	Scalp	1 0.75	30 12	Negative	Negative	Recovered
6	M	Congenital cerebral maldevelopment	9	Positive	T. tonsurans	6	Scalp	1 0.5	30 12	Negative	Negative	Recovered
7	M	Cerebral birth trauma	7	Positive	M. audouini	6	Scalp	2 0.5	30 12	Negative	Negative	Recovered
8	M	Congenital cerebral maldevelopment	8	Positive	T. tonsurans	6	Scalp	1 0.5	30 12	Negative	Negative	Recovered
9	M	Cerebral infection, postnatal meningitis	10	Positive	T. tonsurans	6	Scalp	1 0.75	30 12	Negative	Negative	Recovered
10	M	Cerebral birth trauma	9	Positive	M. audouini	6	Scalp	1 0.5	30 12	Negative	Negative	Recovered
11	M	Postinfection	13	Positive	No culture growth	8	Scalp	1 0.75	30 12	Negative	Negative	Recovered
12	M	Congenital cerebral maldevelopment, familial	11	Positive	T. tonsurans	6	Scalp	1 0.5	30 12	Negative	Negative	Recovered
13	M	Congenital cerebral maldevelopment with tuberous sclerosis	10	Positive	M. audouini	6	Scalp	1 0.5	30 12	Positive	Positive for M. audouini	Direct microscopic examination negative after 16 wk. of treatment; results of culture pending
14	F	Congenital cerebral maldevelopment, indeterminate	10	Positive	T. tonsurans	8	Scalp	1 0.5	30 12	Negative	Negative	Recovered
15	F	Cerebral birth trauma	7	Negative	No growth	8	Scalp	1 0.5	30 12	Negative	Negative	Recovered
16	M	Congenital cerebral maldevelopment, nonspecific	11	Positive	T. tonsurans	6	Scalp and body	1	42	Negative	Negative	Recovered
17	F	Congenital cerebral maldevelopment, nonspecific	10	Positive	T. tonsurans	8	Scalp	1 0.75	30 12	Negative	Negative	Recovered
18	F	Congenital cerebral maldevelopment with mongolism	12	Positive	No growth	8	Scalp	1 0.75	30 12	Negative	Negative	Recovered
19	F	Congenital cerebral maldevelopment with tuberous sclerosis	9	Negative	No growth	8	Scalp	1 0.75	30 12	Negative	Negative	Recovered
20	F	Cerebral birth trauma with postnatal infection	13	Positive	No growth	24	Scalp	1	42	Negative	Negative	Recovered
21	M	Kernicterus	6	Positive	No growth	6	Scalp	1 0.5	30 12	Negative	Negative	Recovered
22	M	Congenital cerebral maldevelopment due to prenatal infection	7	Positive	T. tonsurans	6	Scalp	1 0.5	30 12	Negative	Negative	Recovered
23	M	Congenital cerebral maldevelopment, nonspecific	18	Negative	C. parakrusei	120	Feet	1	42	Negative	Negative	Recovered
24	F	None	46	Positive	M. canis	4	Scalp and body	2 1	42 *	Negative	Negative	Clinically cured after 3 wk. of treatment; refused to cut hair; condition recurred 3 wk. after treatment stopped
25	F	Diabetes	44	Positive	T. schoenleini	114	Scalp	1	*	Positive	Positive	No fluorescent hairs after 90 days; culture positive on 58th day of therapy
26	M	None	10	Positive	T. violaceum	24	Scalp	1	75	Positive	Positive	Recovered in six weeks
27	M	None	38	Positive	T. rubrum	240	Nails	1	92*	Positive	Positive	Increasingly larger zone of normal nail distal to cuticle; culture positive on 58th day of therapy
28	M	Congenital cerebral maldevelopment with mongolism	52	Positive	T. rubrum	†	Body and nails	1	70	Body—Neg. Nails—Pos.	Body—Neg. Nails—Pos.	Body lesions cleared in 10 days; increasingly larger zone or normal nail distal to cuticle
29	F	Congenital cerebral maldevelopment, indeterminate	11	Positive	T. tonsurans	9	Scalp	1	42	Negative	Negative	Clinically well
30	M	Congenital cerebral maldevelopment due to prematurity	16	Positive	M. canis	8	Scalp	1	42	Negative	Negative	Clinically well
31	M	Congenital cerebral maldevelopment with mongolism	27	Positive	T. rubrum	12	Nails	1	42*	Positive	Positive	Increasingly larger zone of normal nail distal to cuticles
32	M	Congenital cerebral maldevelopment, indeterminate	28	Positive	T. rubrum	12	Nails	1	42*	Positive	Positive	Increasingly larger zone of normal nail distal to cuticles

* Patient still on therapy at time of writing.
† Duration of several years.

per kilogram of body weight. A hint of possible toxic effect, with a dose far in excess of that which will probably emerge as the optimum therapeutic dose in humans, was noted after a single intravenously given dose of 100 to 200 mg. per kilogram. They also gave, intraperitoneally, 2 Gm. per kilogram to another group of Wistar rats. In the former group, six hours after administration, arrest of mitotic activity occurred, particularly in the marrow and the intestine. In the latter group, after daily medication for four days, the rats were killed on the fifth day and examined histologically. Seminal epithelium was found to be severely damaged and completely necrotic in many places.

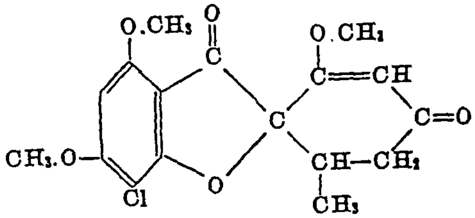

Fig. 1.—Structural formula for griseofulvin.

Methods

Diagnosis was established in each case by (1) direct microscopic examination of suspected hair, skin, or nails and (2) culture. All of our patients had been treated intensively with conventional local medication and had had indifferent to negative results. Local medication was stopped in all cases a few days prior to initiation of griseofulvin therapy. One patient (case 25), with favus, had had no treatment of any kind for 10 years (fig. 2). In the patients with tinea capitis, the hair was cut short on the 28th day, except in two patients (cases 24 and 25).

Prior to the beginning of medication the following studies were made: complete blood cell count (weekly); routine urine examination (weekly); marrow examination; blood urea nitrogen, serum creatinine, and serum uric acid level determinations; cephalin flocculation determination; thymol turbidity test; testicular biopsy specimen studies (two cases); and electrocardiographic, electroencephalographic, and psychological studies. The same studies were made after 28 days of medication. As indicated, some of the tests were repeated weekly. The table gives the concomitant diagnoses, the ages of the children (inmates at the Austin State School), duration and site of infection, type of fungus, drug dosage, duration of therapy, and results. Photomicrographs of testicular biopsy specimens taken from one patient (case 16) the day before therapy was started and on the 28th day of treatment are shown in figure 3. Paget and Walpole[8] had stated that recovery of hematopoietic tissue in animals occurs rapidly 24 hours after cessation of medication, although evidence of testicular damage is discernible for 10 days after a single massive dose has been given.

The types of dermatophytes in our study were as follows: Microsporum audouini (5 cases), Microsporum canis (2 cases), Trichophyton tonsurans (12 cases), Trichophyton violaceum (1 case), Trichophyton schoenleini (1 case) (same as previously reported by one of us with Eppright[9]), Trichophyton rubrum (4 cases), and Candida parakrusei (1 case).

Two patients with apparent tinea capitis (cases 15 and 19), clinically, gave consistently negative results of direct microscopic examinations and negative cultures from the beginning of the series. Medication was continued in these two cases and clinical improvement was noted. Four patients (cases 11, 18, 20, and 21) showed positive results of direct microscopic examinations but negative cultures from the beginning of the series. In one patient (case 23) who produced a culture positive for C. parakrusei, no improvement was seen after griseofulvin therapy, and local therapy with nystatin (Mycostatin) caused the lesions to clear.

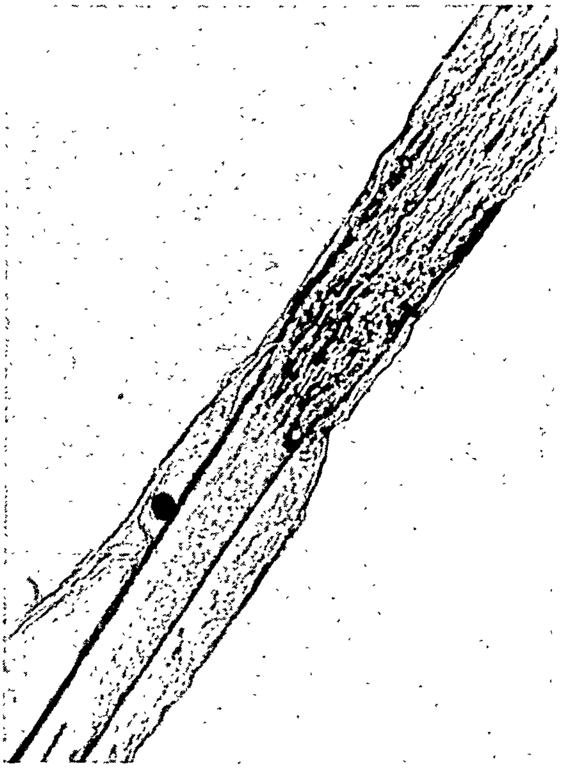

Fig. 2 (case 25).—Hair showing Trichophyton schoenleini infection, with free zone at left and mycelia and spores at distal portion on right.

Therapeutic Results

Since we are dealing with a new therapeutic agent, it is evident that claim of cure must be guarded. It is our plan to follow up our patients for at least six months for evidence of relapse. Since both direct microscopic examinations and cultures gave negative results in cases 15 and 19, these, of course, cannot be considered in this section of the report, even though clinical improvement was noted.

Medication was stopped in all of the children at the Austin State School at the end of the sixth week, except in one patient (case 13). Then their heads were shaved. Medication was stopped for patients in whom direct microscopic examination and examination with the Wood's light showed negative results. The heads of all children were shaved again 14 weeks after therapy was begun; one patient (case 13) was still producing fluorescent and microscopically positive hairs.

At the time of this writing, a patient (case 27) with T. rubrum infection of the nails is showing an increasingly larger zone of presumably normal nail distal to the cuticle. Scrapings and cultures from the infected portions are still positive.

The patient (case 26) with T. violaceum infection began to show a "free" zone after two weeks of medication. Because the hairs broke off so readily (at the juncture of the free zone and normal hair), hair stumps positive for fungus, from then on, were increasingly difficult to demonstrate. His head was shaved at the sixth week. Since that time no hairs positive for fungus have been found. There was no growth on a culture taken one week after shaving the head.

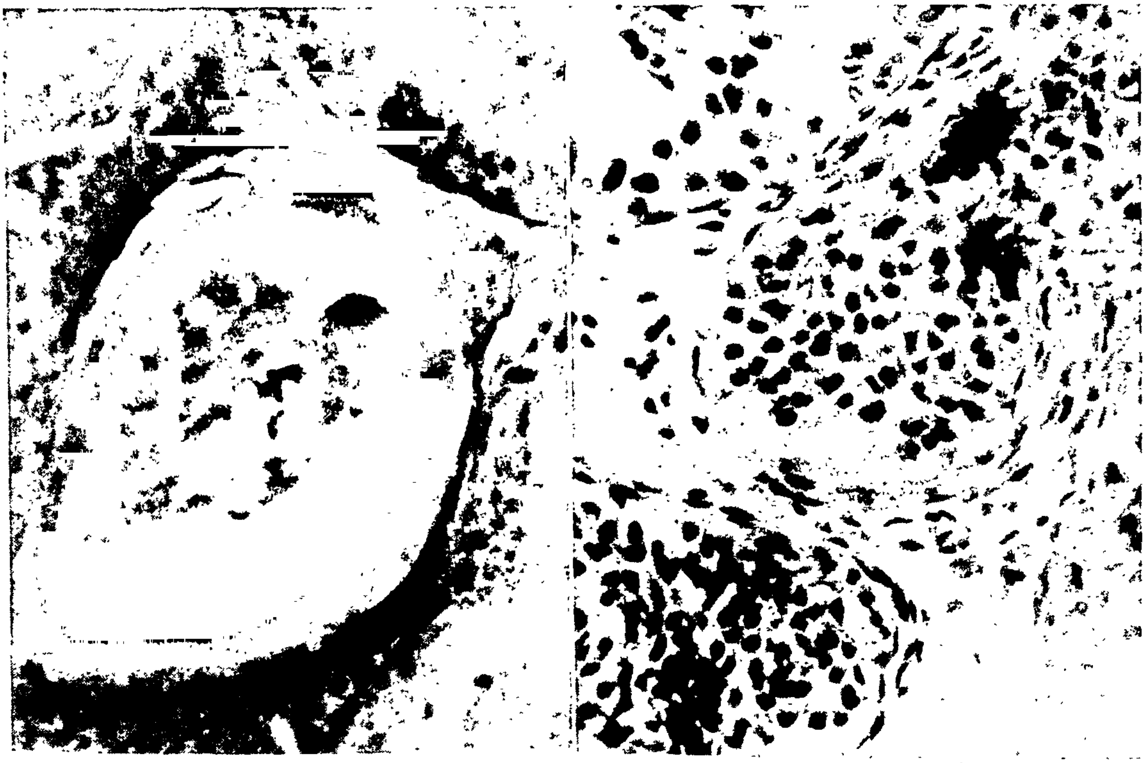

Fig. 3 (case 16).—*Left,* testicular biopsy specimen taken prior to medication. *Right,* testicular biopsy specimen taken on 28th day of medication.

The patient (case 24) with M. canis had many circinate lesions on the body as well as the scalp. The body lesions had cleared completely within 10 days after therapy was started, and there has been no recurrence. After three weeks of medication no fluorescent hairs could be found. This patient was most averse to cutting her hair. She diligently and vigorously washed her hair and presumably broke off the infected portions thereby. Three weeks after medication was stopped, two scaly areas in the scalp appeared. Hairs examined therefrom were positive for Microsporum. Medication was resumed.

One patient (case 28) had severe involvement of the trunk, groin, and thighs, as well as all nails except those of the right hand. Ten days after the beginning of medication, all lesions, except those of the nails, had cleared completely. At that time there was no noticeable change in the involved nails. After five weeks of medication an apparently normal nail was beginning to appear at the proximal ends.

The patient (case 25) with T. schoenleini infection has been the most interesting of all to observe. Hairs infected with this particular fungus do not break off easily. Prior to therapy, most of the hairs of the patient's scalp were fluorescent and microscopically positive for fungus throughout their entire length (up to 12 in.). At the end of two weeks of therapy, the proximal portions of most hairs were observed to be nonfluorescent and microscopically negative (fig. 2). This patient also was adamant about cutting her hair. When the normal portion of the hair became about 3 in. long, the hairs were then cut proximal to the free zone, i. e., in the presumably noninfected portion. At this writing, no more fluorescent hairs are to be found.

Toxicology

In analyzing the toxicology data mentioned in the section on "Methods," all test results, with the exception of the differential counts, were unchanged during the course of treatment. It was noted that there was a tendency toward a right shift in the peripheral counts during treatment; this was analyzed statistically to determine its significance, with use of the "t" test.[10] It was found to be of slight statistical significance; however, analysis of the peripheral white blood cell counts and myeloid-erythroid ratio revealed no significant difference in pretreatment and post-treatment results. Since a change of this type involving no suppression of the marrow and an absolute increase in the lymphocytes is not compatible with our knowledge of hematology today, the explanation for this finding is not apparent.

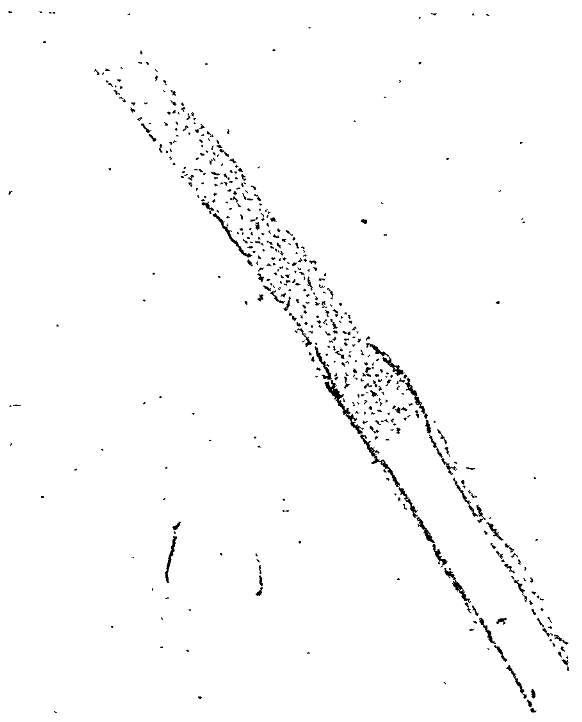

Fig. 4.—Infected hair, showing proximal free zone at right of shaft. (Published with permission of Dr. J. L. Pipkin and Dr. John Ferguson.)

For two patients, testicular biopsies were done before and after 28 days of treatment. None of the biopsy specimens showed any abnormality (fig. 3).

Electrocardiograms were obtained in all instances, except in cases 27 and 28, before and after four weeks of treatment. Comparison of the two sets of tracings revealed no change in electrocardiographic pattern in any instance. Electroencephalograms were taken in a group of 25 patients at the Austin State School before and after 28 days of therapy. Eleven patients had readable tracings, and no patient exhibited any abnormality due to the griseofulvin treatment.

Behavioral observations were done on 22 of the mentally retarded patients, with use of statistics obtained from data on rating sheets for each of the subjects. Each child was rated against changes in his own behavior two times a week for a one-month period of treatment. Statistical analysis with use of the "t" test [10] showed no significant changes in behavior while the patient was under treatment.

Complicating Illnesses

One patient (case 15) suffered from an iron deficiency anemia of mild to moderate degree, thus causing her myeloid-erythroid ratio to be slightly low (1.5/1).

A marked eosinophilia involving the marrow as well as the peripheral count was noted in one patient (case 22). A stool specimen for ova and parasites revealed that he had a Strongyloides stercoralis infestation, which we felt accounted for this abnormality.

In case 25 the patient was found to have mild diabetes prior to the initiation of therapy. This was easily controlled while the patient was on griseofulvin therapy.

Case 28 was interesting in that the patient, on the 48th day of treatment, developed severe erysipelas of the face and cellulitis of the feet. Staphylococcus aureus was isolated. The patient was seen and treated at another institution; the infection was promptly controlled with penicillin, streptomycin, erythromycin, and kanamycin. The intervention of this infection suggests that griseofulvin had no antibiotic effect against Staphylococcus aureus. It is interesting to note that the significant right shift in the differential counts observed in this series was noted to a mild degree in counts done on this patient 14 days before the onset of the infection; however, the differential count was normal 12 days before the infection began, and the patient had a left shift with leukocytosis (white blood cell count of 18,050 per cubic millimeter) on the day the infection was noted. In this case, the ability to produce a left shift with infection was not impaired by treatment with griseofulvin.

Comment

Certain phenomena or behavior patterns of the infection were observed in many of our patients during treatment. Although we are not certain of their significance, we feel that their presence is worth mentioning.

In all of the patients with tinea capitis, except those with M. audouini (case 13), T. schoenleini (case 25), and T. violaceum (case 26), at about the 10th day of treatment few spores were seen on direct microscopic examination. Instead, mycelia were growing luxuriantly around the hair shaft and in the debris attached thereto. In the cases in which more strict hygienic standards were used, this phase gradually disappeared; later, in the proximal part of the infected portion of the hair, fragmented mycelia were the rule. In the cases of less strict hygienic care of the scalp, the phase of mycelia growth and final diminution and fragmentation ensued but was of longer duration.

One possible interpretation of this phenomenon is that griseofulvin, while allowing the spores to proceed to their vegetative, mycelia form, prevents the completion of the cycle from mycelia to spores. This would suggest that the treatment-resistant spore is made vulnerable to directly applied fungicides.

Depending on the rate of hair growth, after one to three weeks of medication, a nonfluorescent, apparently normal portion of hair could be seen emerging from the scalp which we referred to as the free zone (fig. 4). Unlike the ordinary tinea-infected hair, which epilates so easily, such hairs seemed firmly imbedded and pulling of same was painful to the patient. This free zone was especially noticeable in the patient with favus infection (case 25); the infected hairs, when first observed by us 12 years prior to this writing, were fluorescent throughout their entire length of 8 or 10 in. In this case, the infected portion (purposely) was not clipped off until the free zone was over 3 in. in length (fig. 1).

After about the second week of medication, many fluorescent hairs were seen which plucked with difficulty and pain to the patients. Often, the fluorescent portion would "shuck off" like a glove. The sheath which slipped from the hair and seemed like powder was soluble in 20% potassium hydroxide solution and, on microscopic examination, contained no spores or mycelia. The chemical content of this sheath is not known to us, but its fluorescence was indistinguishable from that of actually infected hairs.

One patient (case 13) with M. audouini remained clinically infected with hairs which became duller in fluorescence (almost brick red), and fragmented mycelia (no spores) were seen even in the portion of the hair next to the papilla, with numerous mycelia outside the hair shaft until the end of 16 weeks of therapy. At the time of this writing the patient is clinically well with no fluorescent hairs and a negative result of direct microscopic examination; culture studies are pending.

It was interesting to note that griseofulvin, in the doses used, produced a mild but significant right shift in the differential counts without any significant change in myeloid-erythroid ratio or the total white blood cell counts. Therefore, it would seem that the relative decrease in number of segmented cells occurs outside the marrow. It is recommended that any patient being treated with this preparation be followed closely in regard to differential counts.

Summary

Thirty-two patients with superficial fungus infections were treated with griseofulvin. All except three patients, who had involvement of the nails only, had tinea capitis or mixed tinea capitis and tinea corporis. Treatment of the tinea capitis and tinea corporis infections resulted in cure in all except one case. This patient had a Microsporum canis infection and refused to cut her hair. Infection was noted to recur three weeks after therapy was discontinued. There have been no other occurrences of fungus infections in the treated patients since the drug therapy was discontinued. The three patients with onychomycosis are still under treatment at this writing, and the proximal portions of their nails appear normal. One patient with a Candida parakrusei infection of the feet was also treated with griseofulvin, but treatment was a complete failure.

Toxicological studies included complete blood cell counts and urinalysis before and at weekly intervals during the therapy. Complete blood cell counts were repeated six weeks after therapy was discontinued. Also determined were cephalin flocculation, thymol turbidity, and blood urea nitrogen, blood uric acid, and blood creatinine levels before treatment and after 28 days of treatment. Marrow examinations were done before and after 28 days of treatment and six weeks after the drug therapy was discontinued. Electrocardiograms and electroencephalograms were taken before and after 28 days of treatment. Behavioral observations were done on the mentally retarded patients before and during treatment. The only significant effect noted was a right shift in the peripheral blood cell count which began after drug was used. The total white blood cell counts were not significantly changed during therapy but showed a significant rise six weeks after therapy was discontinued. There was no significant alteration in the myeloid-erythroid ratio in the marrow.

Complicating illnesses included an iron deficiency anemia of moderate degree in one case, a case of Strongyloides infestation which exhibited a marked eosinophilia secondary to infestation, and a case of mild diabetes discovered at the onset of therapy. The diabetes was easily controlled during the course of therapy. One patient (case 28) developed a staphylococcic infection of his face and foot on the 48th day of treatment but responded to antibiotic therapy promptly. It is interesting to note that griseofulvin had no antibiotic effect against the staphylococcic infection and that patient had a marked left shift during the infection in spite of the fact our studies showed some tendency to a right shift in the peripheral blood cell counts.

Griseofulvin is an effective antibiotic for superficial fungus infections and is safe in therapeutic doses. No instance of intolerance to griseofulvin requiring reduction of the dosage or cessation of administration of the drug was encountered.

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Dr. Samuel Hoerster, Mr. E. W. Killian, Dr. Sidney Bohls, Mr. Harold Bredhauer, Dr. John Boston, Mrs. Nadea Giezelbach, and Dr. Charles Pelphrey assisted with the clinical studies in this report.

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CURRENT STATUS OF LIVE POLIOVIRUS VACCINE

Leroy E. Burney, M.D., Washington, D. C.

A considerable fund of information has been accumulating on the properties of live-virus poliomyelitis vaccines and on the use of these vaccines in human beings. The recent publication of the proceedings of the conference on live poliovirus vaccines, held in Washington, D. C., June 22-26, 1959, under the auspices of the World Health Organization and the Pan American Health Organization, provides a good opportunity to review the current state of knowledge.

The proceedings contain progress reports on field studies of these vaccines now under way in countries in Europe, Asia, and South America. Great numbers of people have been vaccinated in the U. S. S. R. and elsewhere. In general, the reports indicate a good record of safety for the vaccines under trial, although the extent of surveillance and follow-up study is somewhat unclear.

The attenuated live viruses used in these vaccines have lost the power to produce disease through a process of selective cultivation in the laboratory. They can, however, be transmitted by persons who have ingested them to others through natural means. On this point, the conference report noted, "The use of a product that spreads beyond those originally vaccinated represents a radical departure from present practice in human preventive medicine."[1]

It has been maintained that this might be a useful characteristic under certain circumstances, i. e., if there were assurance that the virus would remain in an attenuated state after passage through the human intestinal tract. A number of reports presented at the conference, however, including those of Melnick, Verlinde, Smorodintsev, and Stuart-Harris, indicated a potential in at least some of the vaccine viruses under consideration for reversion to virulence. This suggests a strong need for further study of the vaccines before they can be recommended for general use. The problem of reversion to virulence has been highlighted again in a recent report by Melnick and co-workers.[2]

The principal problem, therefore, in evaluating the ultimate safety of live poliovirus vaccines is the possibility of the spread of virus, coupled with its potentiality for reversion to virulence.

In June, 1958, the Public Health Service established a committee on live poliovirus vaccines,

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composed of experts in the fields of virology and immunology from within and outside the government. This committee has been closely following developments relating to live-virus vaccines, both in the laboratory and in field trials in various parts of the world. The group recently drafted recommendations[3] pertaining to the problems which must be solved before licensing of a commercially produced vaccine can be considered.

In addition to providing satisfactory results of field trials a vaccine designed for general use must meet certain laboratory tests. Such tests represent the only experimental criteria available for the continued control of individual lots of vaccine as they are produced by the manufacturers.

One criterion is based on the vaccine's degree of neurovirulence for monkeys. As the recent conference report disclosed, results obtained by different investigators have varied considerably. In order to obtain comparative information on the three sets of strains (Sabin, Cox, and Koprowski) in the experimental vaccines, the Division of Biologics Standards, which administers the Public Health Service's responsibilities in the field of biologicals control, carried out studies of these strains under standardized conditions. The data showed that there is considerable difference among the three sets of strains, from the point of view of their neurovirulence in monkeys, as determined by histological lesions and paralysis occurring after intracerebral and intraspinal inoculation.[4] These results are also in agreement with those of Melnick and co-workers.[2]

The committee on live poliovirus vaccines therefore recommended that a virus strain be considered satisfactory only if its neurovirulence as tested by the recommended procedures is low. In addition, the committee agreed that live-virus vaccine strains must also demonstrate inability to revert to significant neurovirulence after passage in human beings.

Each lot of vaccine produced must be shown to possess the same genetic markers as the seed virus. These genetic markers are inherent properties of a virus strain. If the markers of an individual lot of vaccine differ from those of the seed, that lot should not be used for immunizing human beings. A number of the markers are determined by studying characteristics of virus strains in tissue culture. One such characteristic, called the temperature (t) marker, involves the growth of the virus at higher temperatures, such as 40 C (104 F). The virulent virus generally grows well at this temperature while the avirulent virus grows poorly, thus providing an element of discrimination. Another characteristic is the ability of the virus to grow when only a small amount of sodium bicarbonate is present in the tissue culture medium. A third characteristic is the MS (monkey-stable) marker, involving cultivation on a stable, continuous, tissue-culture cell line derived from monkey kidney.

The determination of a number of these, and perhaps other, markers is essential in order to differentiate between the attenuated and the virulent or wild strains.

A realistic consideration of these and other problems makes it difficult to predict when a live poliovirus vaccine could be licensed for commercial production. The Division of Biologics Standards has met with the vaccine developers and with interested manufacturers as a step in establishing standards for safety and for production of such vaccines. The Public Health Service cannot recommend the licensing of such a biological product until the manufacturer has demonstrated not only the safety and potency characteristics of the vaccine strains but also his ability to meet established standards for successive production lots of vaccine.

Summary

The Public Health Service has a considerable interest in the development of live poliovirus vaccine. This interest arises both from its concern with preventive measures and from its legal responsibilities for the licensing of biological products. A continuing review of progress has been made by the PHS committee on live poliovirus vaccine. This review indicates important progress toward the development of a safe and effective poliomyelitis vaccine for oral use. Some important safeguards will need to be developed before there can be full assurance concerning the safety and potency of these products for general use by the physician.

When the scientists and public health physicians of the United States and other countries have provided evidence of safety and of lack of significant reversion to virulence of the vaccine strains, on the basis of both laboratory and field experience, and when proper manufacturing safeguards have been satisfactorily established by the vaccine manufacturers the Public Health Service will act on applications for the licensing of live poliovirus vaccine. In the meantime, there should be no abatement of full use of the demonstratedly effective Salk vaccine.

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VASCULAR MEASUREMENTS OF SMOKERS AND NONSMOKERS

DIFFERENCES SEEN IN POSTEROANTERIOR ROENTGENOGRAMS MADE WITH PATIENTS STANDING ERECT

Josue Pagan-Carlo, M.D., New Orleans

Plain anteroposterior roentgenograms of the chest were used to obtain micrometric measurements of the caliber of the pulmonary blood vessels. The arterial shadows were classified by location as main hilar, perihilar, midzone, and peripheral, and the average diameters of each class of arteries were noted in 257 nonsmokers, 133 light smokers, 204 moderate smokers, and 100 heavy smokers, in order to see whether smoking had measurable effects on the pulmonary circulation. The most striking difference was in the size of the main hilar vessels, namely, 0.533 in. for nonsmokers and 0.664 in. for heavy smokers. The difference, significant by statistical criteria, was interpreted to indicate hypertrophic dilatation of the pulmonary arteries. This could be explained by assuming that vasoconstriction or spasm in the smaller arteries or arterioles was precipitated by the chronic action of nicotine, since the vasoconstrictive effect of that drug is well known and easily demonstrated.

The effect of tobacco smoke on the respiratory tract of man has been the subject of intense and deliberate investigation in the past few years, as a result of the apparent causal relationship between smoking and pulmonary or bronchogenic carcinoma. The incidence of pulmonary carcinoma in heavy smokers, as well as their death rates, has been studied repeatedly by means of statistical methods, with interesting and controversial conclusions on the possible carcinogenic effect of tobacco smoke.[1] Certain reports on the histopathological changes in the bronchial epithelium of heavy smokers have added some weight to the arguments in favor of such effect, but there is no general agreement about the interpretation of such findings.[2]

The vascular pattern of the lungs in the plain posteroanterior chest roentgenograms, made with the patients standing erect, of smokers and nonsmokers were studied in an attempt to establish any changes in the vascular shadows of the lungs. The effect of smoking on the cardiovascular system of man has been studied and is well known; however, to my knowledge no attempt has been made to detect any significant change in the caliber of the arterial shadows in the chest roentgenogram.

Method

The present study deals with micrometric measurements of the vascular shadows in the right middle and lower lobes on the routine chest roentgenograms of 694 asymptomatic smokers and nonsmokers. The measurements were performed by means of a vernier caliper calibrated to 1/1,000 in.

The right middle and lower lobes were divided arbitrarily into four main zones: (1) hilar, consisting of the distal end of the descending branch of the right pulmonary artery, and the distance between the above-mentioned point and the right costophrenic angle then being divided into three equal portions corresponding to (2) perihilar, (3) midzone, and (4) peripheral.

The following classification of subjects was used in the tabulation of the results: (1) nonsmokers (257), (2) light smokers—10 cigarettes or less daily (133), (3) moderate smokers—over 10 but less than 30 cigarettes daily (204), and (4) heavy smokers—more than 30 cigarettes daily (100). It may be well to emphasize that the measurement of the vascular shadows in the peripheral zone was quite difficult; the average measurement of the smallest visible branches was used. Accurate measurements were possible in the hilar, perihilar, and midzone areas; however, some difficulty was encountered with the measurements in the hilar area of some patients, because of the superimposition of the shadows of the ascending aorta, the right cardiac border, and at times the main bronchus to the right middle and lower lobes.

Results

The average measurements for the hilar, perihilar, midzone, and peripheral arterial shadows for the four groups of patients are summarized in the table.

The statistical analysis for significance in the differences of average measurements of the main or hilar area of patients in the four categories revealed significant findings only when nonsmokers were compared to heavy smokers, in which case an F value [3] of 7.297 was found, as against a required F value of 3.80. Average measurements of the perihilar, midzone, and peripheral areas were higher in the heavy smokers, but there were no significant statistical differences.

J. Aron Fellow, Department of Radiology, Touro Infirmary.

Comment

The analysis of variance in the measurements of the main or hilar trunk suggests the presence of a significant difference between nonsmokers and heavy smokers which could be attributed to the chronic effect of heavy smoking. There appears to be little effect, if any, discernible in the vascular measurements of light or moderate smokers.

The mechanism leading to hypertrophic dilatation of the wall of the distal portion of the descending branch of the right pulmonary artery, as reflected by larger caliber in heavy smokers, is a subject for speculation or theorization. Waldbott[4] found an accentuation of the hilar shadows in the lungs of patients with the so-called smoker's respiratory syndrome.

Grishman and Dack[5] stated that dilatation of the pulmonary artery commonly results from primary or secondary hypertension of the pulmonary arterial circulation. Comroe[6] commented that the pulmonary circulation is not always a low-resistance or low-pressure system. Pathologically it may become a high-resistance or high-pressure system in response to long-continued increased flow, pressure, or obstruction. He added that pulmonary arteries are not devoid of smooth muscle, so that hypertrophy can develop, and finally that they are not lacking in vasomotor regulation, although this control may be effected by stimuli different from those that excite the peripheral systemic circulation.

Burton[7] believed that the hemodynamics of the pulmonary vascular bed must depend on the same factors as those which operate in peripheral vessels, adding that a small degree of vasomotor tone might tend to close these vessels completely, since the arterial pressure needed to keep them open is much less than that in the systemic circulation. Short[8] believed that pulmonary hypertension develops in three stages; first, arterial hypertonus; second, arterial contracture; and third, arterial obstruction.

Motley and Kuzman[9] found that pulmonary compliance measurements made after smoking were consistently and significantly decreased in most subjects, normal ones as well as those with pulmonary emphysema. Grishman and Dack[5] also found that tobacco smoke produced a consistent significant decrease in the arterial blood oxygen saturation in most subjects with severe emphysema; pulmonary compliance measurements made after smoking were consistently decreased in most subjects. According to Dubois[10] an increase in the resistance would raise the pulmonary arterial pressure during flow, and this in turn would distend the pulmonary arterial tree, resulting in decreased pulmonary compliance. The vasoconstrictor effect of nicotine may be a factor in the above-mentioned changes.

Histopathological changes in the lesser arterial vessels of the lungs in subjects with pulmonary hypertension are described as manifestations secondary to the alterations in blood flow, volume, and tension produced by disease of the lungs. These changes consist basically of atherosclerosis of the larger arteries, hypertrophy or at least thickening of the muscular arteries, and fibrosis of the intima in the smaller arteries and precapillary arterioles. The necrotizing vascular lesions are regarded as nonspecific effects of high pressure in the vascular circuit. Silvette and co-workers[11] commented on the fact that tobacco smoke or nicotine influences certain immune reactions; skin reactions to tobacco recorded in the literature provide evidence that skin sensitivity to tobacco extracts may be a true immune reaction. It is possible that an altered state of sensitivity or hypersensitivity to nicotine or tobacco smoke may produce isolated areas of vasculitis or necrotizing arteriolitis. According to Muirhead and Stirman[12] changes in arteriolosclerosis are considered as due to local or regional injury mediated or aggravated by the hypertensive state.

It has been established that the main factor in the pharmacological effect of tobacco smoke on the cardiovascular system is nicotine. The acute effect of nicotine on the cardiovascular system apparently is mediated by the sympathetic nervous system. It has been determined experimentally in man that it produces a definite decrease in reactive hyperemia in the limb, with intact sympathetic innervation, and no change at all in the limb where the sympathetic nervous flow has been cut off.[13] The primary effect of nicotine in the peripheral vascular system is one of vasoconstriction, as manifested by a reduction in the number of nailfold capillaries or loops, increase in pulse rate and blood pressure, and decrease in skin temperature.[14]

*Mean Vascular Measurements of 694 Smokers and Nonsmokers**

Area	257 Non-smokers	133 Light Smokers	204 Moderate Smokers	100 Heavy Smokers
Main hilar	533	530	556	664
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* Measurements in thousandths of an inch, performed in the right middle and lower lobes.

On the basis of existing experimental information, one may theorize that dilatation of the distal portion of the descending branch of the right pulmonary artery in heavy smokers may reflect an altered pressure gradient in the pulmonary arterial circuit, as a result of vasoconstriction or spasm in the smaller arteries or arterioles precipitated by the chronic effect of nicotine. No one knows all the possible reflexes initiated in the lungs as a result of either intrapulmonary or extrapulmonary stimuli, or the effects of the irritating inhalants in the tobacco smoke. However, it has been established that in the development of pulmonary hypertension the basic mechanism appears to be arterial hyper-

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No systematic histological study of the pulmonary arterial tree of heavy smokers has been made, and it would be of interest to everybody concerned that such a study be made, in a reasonable number of cases, in an effort to establish an anatomic basis for the physiological and roentgenographic findings.

Summary

Vascular measurements were performed in the right middle and lower lobes of 694 smokers and nonsmokers. A statistical analytical study was made of the average measurements, which appears to show a significant difference in the measurements (in the main hilar zone) of heavy smokers, as compared to nonsmokers, possibly due to the chronic vasoconstrictive effect of nicotine on the smaller radicles of the pulmonary arterial tree, resulting in some degree of pulmonary hypertension. No significant difference was demonstrable in the vascular markings of light and moderate smokers, as compared to nonsmokers. Basic research in the histopathology of the pulmonary arterial bed of heavy smokers is desirable in order to establish an anatomic basis for the roentgenographic and physiological findings.

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Mr. Caleb Pagan-Carlo, B.S., Ch.E, M.Sc., aided in the preparation of the statistical analysis.

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FATALITIES INVOLVING FIREARMS.—No progress has been made during the past decade in reducing the mortality from firearm accidents in the United States, the annual death rate remaining at the level of about 1.4 per 100,000 population. Reflecting the increase in population, the number fatally injured in such mishaps has risen in the past few years—from little more than 2,100 in 1955 to 2,400 in 1958. It is not generally realized that nearly half of the people killed in firearm accidents sustain their injuries in and about the home. An additional one fifth of the victims lose their lives in forests, uncultivated fields, and like areas, largely in activities associated with hunting and similar sports.—Firearm Accidents Costly in Lives, *Statistical Bulletin Metropolitan Life Insurance Company,* September, 1959.

TRANSMISSION OF NORTH AMERICAN BLASTOMYCOSIS

POSSIBLE CASE OF TRANSMISSION FROM DOG TO HUMAN

Robert M. Schwartzman, Ph.D., M.P.H., V.M.D., Ramon M. Fusaro, M.D.
and
Milton Orkin, M.D., Minneapolis

A 52-year-old man died five or six weeks after the appearance of an inflammatory swelling of his knee. Treatment by aspiration, drainage, and antibiotics had been ineffectual. A mass was visible in early roentgenograms of the chest. Later roentgenograms showed multiple irregular densities scattered throughout both lung fields. After a febrile course the patient died in respiratory failure. Autopsy findings confirmed the diagnosis of North American blastomycosis. Similar history and findings were noted in the case of a dog that had died three months earlier, and the circumstances suggest that the man may have contracted the disease from the dog. Microscopy showed the essential lesions in both the human and the canine patient to be granulomas and demonstrated the presence of Blastomyces dermatitidis.

The purposes of this paper are to (1) draw attention to the fact that the incidence of North American blastomycosis in animals is probably greater than realized; (2) arouse interest, especially among physicians, in the animal reservoir of North American blastomycosis and stimulate epidemiologic investigations to determine the significance of the disease in animals for man; and (3) report a canine and a human case of North American blastomycosis which apparently were related epidemiologically. In the veterinary literature 16 cases of North American blastomycosis were reported as of 1952, and the total has risen to 77 cases since that time.[1] This marked increase in veterinary reports is probably a reflection of greater awareness and interest in the disease by veterinarians and of more accurate diagnostic procedures. The incidence and distribution of the disease in animals are unknown [2] but, on the basis of reported cases, it appears to be most prevalent in the Ohio and Mississippi river basins.[1b] Of the domestic animals, the dog is considered to be the most susceptible to infections of Blastomyces dermatitidis, but there appears to be no age, breed, or sex predilection.[1a]

Canine cases of North American blastomycosis are clinically similar to those in man.[3] They are characterized by fever and debility, with cough, dyspnea, and cutaneous lesions as the outstanding signs. Cutaneous ulcers, furuncles, and subcutaneous abscesses, without regional adenopathy, are common initial signs.[3] Other manifestations, osseous, ocular, and visceral, vary with the area of localization of B. dermatitidis infection, which usually follows hematogenous dissemination from a primary pulmonary infection.[4] In contrast to its course in man, it appears that the disease in dogs progresses more rapidly and that ocular involvement is more common.[3]

Although much has been written about North American blastomycosis, the fact remains that there is little known of its epidemiology. A review of the literature reveals the following pertinent facts. 1. The organisms which infect dog and man are morphologically and serologically identical.[1c] 2. B. dermatitidis has not been isolated from the soil.[5] 3. North American blastomycosis does not spread from man to man.[5] 4. Percutaneous infection can occur.[1a] 5. There are no known instances of transmission of the disease from dog to man.[6]

Although the last statement has been made repeatedly, it is intimated in the literature that this mode of transmission probably occurs.[7] Also, in actual practice, veterinarians often suggest euthanasia for dogs with North American blastomycosis to protect their owners' health. Finally, there is one report [8] which deals with the occurrence of seven canine and three human cases occurring over a three-year period but does not relate them epidemiologically.

To add support to the contention that transmission can occur from animal to man, we are reporting a canine and a human case of North American blastomycosis which appear to be related as to time and locality of infection. Both cases occurred in a small community in northern Minnesota. The canine infection preceded the human by three months and both ended fatally. Friends of the patient owned the involved dog.

Instructor, College of Veterinary Medicine (Dr. Schwartzman); Instructor in Medicine, Division of Dermatology (Dr. Fusaro); and Trainee, National Cancer Institute, and Fellow, Division of Dermatology (Dr. Orkin); University of Minnesota. Dr. Schwartzman is now Assistant Professor, School of Veterinary Medicine, University of Pennsylvania, Philadelphia; Dr. Orkin is now at Oakland Naval Hospital, Oakland, Calif.

Read before the Section on Dermatology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

Report of Cases

Canine Case.—In April, 1958, a one-year-old female Golden Labrador was referred to the Veterinary Clinic of the University of Minnesota by a veterinary practitioner. The animal had a febrile, debilitating disease of one month's duration. In addition, the owner stated that the patient had been coughing and shedding excessive amounts of hair. Cutaneous lesions appeared about two weeks prior to admission. The patient had been treated with penicillin by the referring veterinarian, with no improvement.

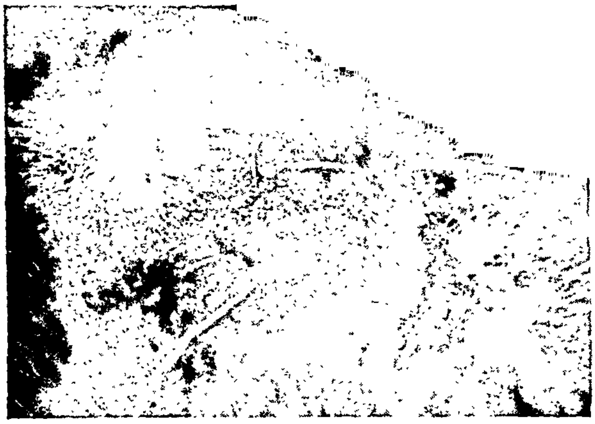

Fig. 1.—Ulcer on right lateral tarsus of canine patient.

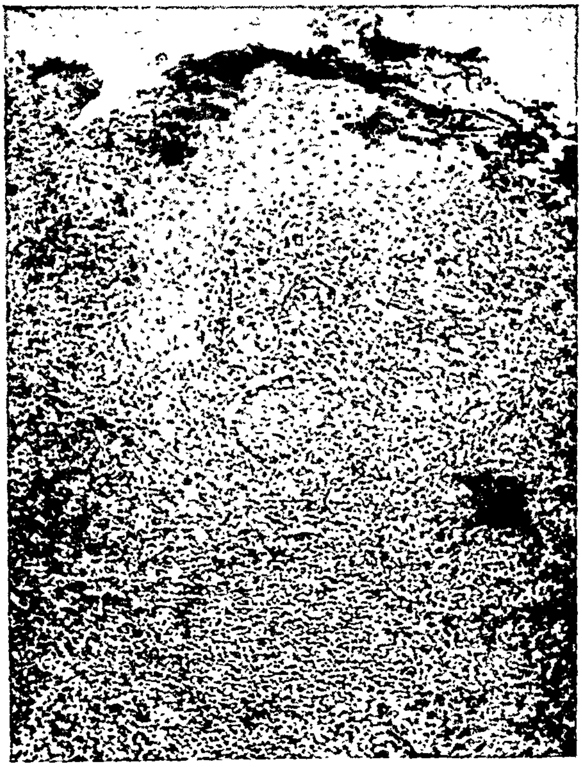

Fig. 2.—Photomicrograph of biopsy specimen from canine patient, showing acanthotic and ulcerated epidermis. Note dense infiltrate through corium (× 24).

Examination of the patient revealed an alert animal in poor bodily condition. The coat was dull. A soft cough was inducible and moist rales were heard on auscultation. The temperature was 105.2 F (40.6 C) (normal 101.4 F [38.6 C]). On the right lateral tarsus there was a circular, nontender, purulent ulcer, 3 cm. in diameter, with an erythematous granular surface and rolled borders (fig. 1). The adjacent soft tissue was swollen but nontender. On the right flank four discrete circular "punched-out" ulcers, 3 mm. in diameter and draining pus, were also present.

Pertinent laboratory data determined on the day of entry included a negative blood culture; the hemogram showed leukocytosis, with a white blood cell count of 41,500 per cubic millimeter (normal 12,000), neutrophilia (but no shift to the left), and an increased sedimentation rate. Roentgenography of the tarsus and chest showed soft tissue swelling of the tarsal area but no bone involvement, bronchiectasis, and resolving bronchopneumonia of the diaphragmatic lobes of the lung. Bacteriological culture of pus showed gram-negative rod-shaped bacteria; mycotic culture of pus showed B. dermatitidis.

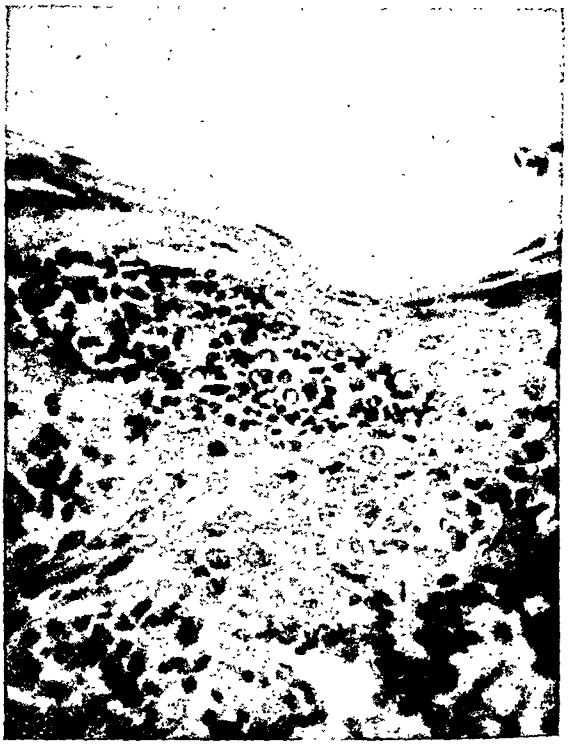

Fig. 3.—Photomicrograph of biopsy specimen, showing intraepidermal abscess. Note double refractile basophilic bodies (× 290).

Biopsy of the tarsal ulcer revealed a purulent crust overlying acanthotic and intermittently ulcerated epidermis (fig. 2). Localized accumulations of polymorphonuclear cells and "double-contoured," basophilic bodies were present in the stratum malpighii (fig. 3). Throughout the corium there was a dense infiltrate consisting of epithelioid cells, polymorphonuclear cells, and occasional giant cells. Vascular dilatation and hemorrhage were prominent. Numerous budding, "double-contoured" bodies (fig. 4, *top*), which stained red-purple with periodic acid–Schiff (PAS) reaction, were present throughout the infiltrate and especially in islands of polymorphonuclear cells (fig. 4, *bottom*).

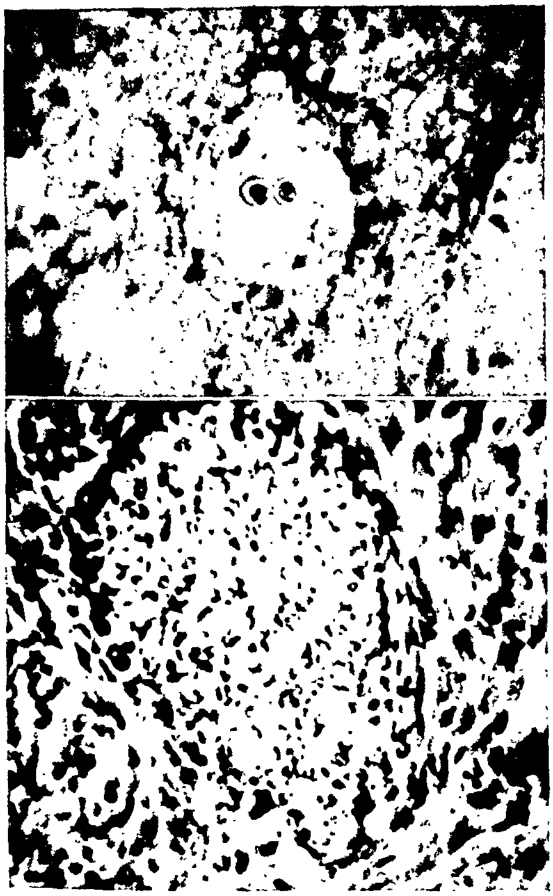

Fig. 4.—Photomicrograph of biopsy specimen, showing B. dermatitidis (*top*) in corium (× 655) and (*bottom*) in island of polymorphonuclear cells (× 290).

During the six days which were required to make the diagnosis of North American blastomycosis the patient's condition did not improve, despite intensive broad-spectrum antibiotic therapy and supportive treatment. Her temperature ranged from 103.2 F (39.6 C) to 106 F (41 C). The attitude of the patient became depressed and her food intake lessened. On the fourth hospital day the patient had an epileptiform convulsion. On the seventh hospital day the owner was informed of the diagnosis and euthanasia was requested. An autopsy was performed and revealed the following outstanding findings.

All lobes of both lungs were moderately congested. Numerous focal and confluent gray-white, relatively firm nodules (2 to 4 mm. in diameter) were present beneath the pleura and within the parenchyma. "Soft" adhesions (early fibrin deposits) were present on the visceral pleura of the right lung and the parietal pleura of the same side. The left lung showed no such change, although a serosanguineous effusion (approximately 100 ml.) was present in the pleural cavities. The tracheobronchial lymph nodes were moderately enlarged and firm.

The meninges, especially over the right cerebral hemisphere, were thickened and opaque, with much fluid, and with blood-tinged gray-white exudate appearing beneath. There appeared to be inflammatory changes and necrosis involving the right cerebrum as viewed on a coronal section. Sections of affected portions of the skin, cerebrum, lungs, and tracheobronchial lymph nodes showed inflammatory changes of a granulomatous nature, with B. dermatitidis demonstrated.

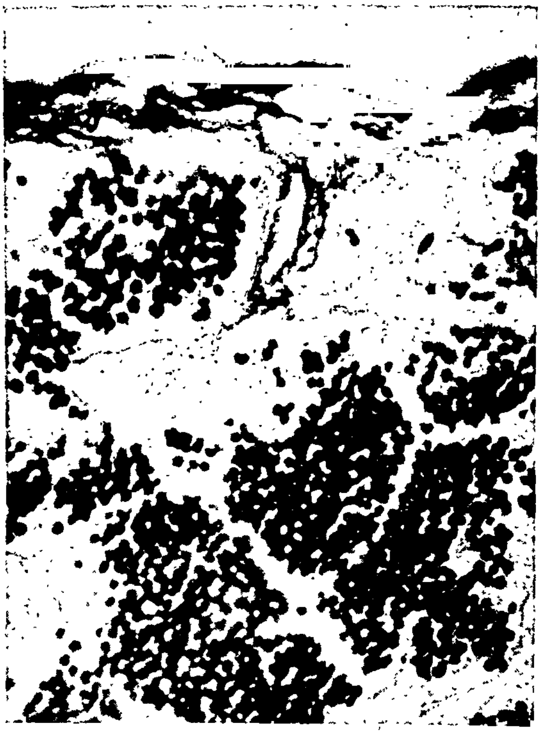

Fig. 5.—Photomicrograph of autopsy specimen from pulmonary alveoli of human patient, filled with B. dermatitidis; PAS stain (× 15).

Human Case.—In early June, 1958, a 52-year-old man was seen by his local physician for a swelling of his left knee. A few days before this he had sustained trauma to his left knee without breaking the skin. During the next three weeks he had several aspirations and incisions of the inflammatory swelling. The patient was placed on therapy with multiple antibiotics, without any change in his condition. A chest x-ray on June 17 revealed a mass in the right hilus and cardiomegaly. During the last week in June he was admitted to a local hospital, and again numerous incisions and drainages were attempted. All cultures were sterile except one from which gram-negative rod-shaped bacteria were grown. While in the hospital he developed an elevated temperature and his general condition became progressively worse. The patient was transferred to St. Luke's Hospital in Duluth, Minn., on July 8 in essentially a terminal state.

The physical examination showed an almost comatose middle-aged man whose respiration was rapid and shallow. The oral cavity contained a large amount of brownish material and the pharynx was moderately inflamed. Auscultation of the chest revealed dulness over both lung bases posteriorly, with many moist rales heard, especially over the right base. There was an edematous and tender swelling below the left knee. No lymph nodes were palpable.

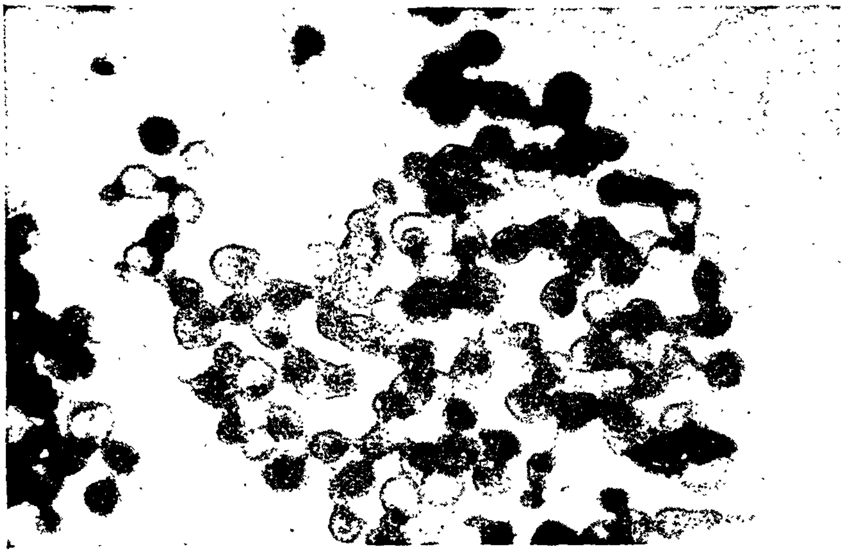

Fig. 6.—Photomicrograph of autopsy specimen from human patient, showing double refractile budding elements in pulmonary alveoli; PAS stain (× 900).

The following results of diagnostic tests performed at St. Luke's hospital were significant: white blood cell count of 13,800 per cubic millimeter, with 92% polymorphonuclear cells, 7% lymphocytes, and 1% eosinophils; hemoglobin concentration, 10.6 Gm.%; sedimentation rate 100 mm. per hour; blood sugar level, 302 mg.%; and blood urea nitrogen content, 18 mg.%. An acid-fast culture of the sputum gave a negative result. Culture of drainage from the left knee yielded only, on one occasion, coagulase-positive staphylococcus. Result of blood culture was negative. Roentgenography of the chest revealed multiple irregular densities scattered throughout both lung fields, suggesting hematogenous metastases or some type of miliary inflammatory process, with no evidence of consolidation. Roentgenography of the left knee was noncontributory.

During the next few days the patient's condition deteriorated, with a marked increase in respiration, elevated temperature, and deepening coma. On July 14, 1958, the patient died, exhibiting signs of marked respiratory failure just prior to death. During the hospital course the patient had received treatment with penicillin, streptomycin, isoniazid, and many broad-spectrum antibiotics. In the terminal phase sulfadiazine and heparin also were given, since multiple pulmonary emboli and nocardiosis were suspected.

Autopsy examination revealed the following significant findings. Numerous individual nodules, 7 to 10 mm. in diameter, were scattered over most of the lung parenchyma. The lungs were of a doughy consistency. The bronchi of both lungs had an inflamed red mucosa which in some areas was gray-white. The lumina of the bronchi were filled with some mucous matter. Focal areas of necrosis and liquefaction were present in the most densely infiltrated areas of the lung parenchyma. There was extensive suppurative destruction of the soft tissue of the left knee and on exposure of the knee joint marked granulation tissue was observed.

Examination of microscopic sections of the lung revealed a chronic inflammatory infiltrate consisting mainly of epithelioid cells and a few giant cells. Focal areas of necrosis were present, especially in the centers of the granulomas. The alveoli were filled with numerous large "double - contoured" spherical elements (fig. 5 and 6). In a few areas definite budding was observed. Sections of the pulmonary hilar lymph nodes were essentially the same. The tissue from the knee joints showed marked necrosis and areas of granulation tissue, with typical blastomyces buds. Cultures of the blood, lung, and left knee were negative for acid-fast organisms, and cultures for fungi which were attempted 24 hours after the time of death were negative. The sections were reviewed at St. Luke's Hospital by Dr. Goldschmidt and at the Mayo Clinic by Dr. Lyle A. Weed, who both agreed on the histological diagnosis of North American blastomycosis.

Comment

The most interesting aspect of this report is the consideration that the two cases are related epidemiologically and represent an example of transmission of North American blastomycosis from a dog to a human being. Such a contention necessitates a discussion of the known possible modes of transmission.

There are no known cases of man-to-man transmission. Also, clinical experience, such as unrestricted handling of patients, supports the fact that man-to-man transmission does not occur. It would seem improbable, therefore, that the man contracted his infection from another person.

There is nothing known of the mode of transmission of North American blastomycosis as related to the dog. It would seem improbable, though, that the dog contracted the disease from the man, since the dog's illness preceded the man's by a period of three months.

That the two cases are totally unrelated, man and dog having become infected from different sources, is unlikely, because both patients had a relatively rare disease in the same locality and within three months of each other. The probability of such a coincidence would appear to be small.

*Results of Intradermal Tests and Chest Roentgenograms of Family Owning Dog**

		Owners of Dog		Children of Owners		
Sex		M	F	M	M	F
Age		45	43	15	13	18
Test Result	Time, Hr.					
Mantoux	48	—	†	—	—	+
	72	—	†	—	—	+
Blastomycin	48	—	±	±	±	±
	72	—	±	—	—	—
Histoplasmin	48	+	±	±	±	+
	72	—	—	—	—	+
Coccidiodin	48	—	±	±	±	+
	72	—	—	—	—	+
Chest x-ray	48 72	normal	‡	normal	normal	normal

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* Test results were all read in mid-May, 1958.

† Mantoux test not done because of previous violent 4+ reaction.

‡ Chest x-ray showed old healed primary lesions in apexes.

Parenthetically, it should be noted that the man probably did not contract the disease percutaneously (after the trauma to his knee), since there was no evidence of regional adenopathy.

The only two remaining possible modes of transmission of infection are to both man and dog from a common source and from dog to man. Both infer that an epidemiologic relationship exists between the two cases, and it is our contention that the occurrence of a canine and a human case of a relatively rare disease, in the same locality and within three months of each other, supports such a relationship. However, without knowledge of the natural habitat of the organism or the degree of contact between the two patients, we believe that it is impossible to state whether animal-to-man transmission occurred or whether both patients were exposed to a common source of infection. Unfortunately, our epidemiologic investigation was restricted to immunological testing of the family that owned the dog. The results of that testing are summarized in the table.

It is to be noted that the mother was the only member of the family who had a positive blastomycin skin test result after 72 hours. Assuming canine-to-human transmission one might expect this, because in most families the mother or wife has the major responsibility of caring for the dog and often the greatest contact with it.

Although man-to-man transmission apparently does not occur, it does not follow necessarily that animal-to-man transmission is not possible. Although the question of animal-to-man transmission of North American blastomycosis remains unanswered, this report should arouse serious consideration of its possibility. It is evident that veterinarians must find out more about the incidence of this disease in animals. It is also imperative that, when physicians make a diagnosis of North American blastomycosis, they request veterinarians to perform the following procedures on their pets and live-stock: (1) complete physical examination, (2) roentgenologic examination of the chest, (3) culture of any cutaneous lesions for fungi, and (4) immunological tests, including triple fungus skin tests and blastomycosis complement-fixation test.

Drs. Cyrus C. Brown, Department of Medicine, and James L. Tuura, Department of Dermatology, Duluth Clinic, and Volker Goldschmidt, Chief of Pathology, St. Luke's Hospital, Duluth, Minn., supplied data pertaining to the human case. Drs. Francis W. Lynch, Director of the Division of Dermatology, and Robert W. Goltz, Clinical Assistant Professor, Division of Dermatology, University of Minnesota, aided in the preparation of this report.

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PREVENTIVE MEDICINE—ITS CHANGING CONCEPTS, 1859-1959

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Since 1859 there has been a section of the American Medical Association, with various names and with varying emphases, devoted to meteorology, medical topography, epidemic diseases, hygiene, sanitary science, industrial medicine, public health, and preventive medicine. The history of the section reflects the changes resulting from the solution of old problems and the emergence of new ones. Important advances resulted from the indentification of parasites and vectors concerned in transmissible diseases, the discovery of methods of immunization, the recognition of deficiency diseases, and the development of chemotherapy. New problems arise from the pollution of air and water by an increasingly dense population, the increase in the average age of the population, the constant introduction of new chemicals and processes into industry, and the accumulating exposure to ionizing radiations. In view of the accomplishments of the past, it is stimulating to consider the problems that lie ahead.

A centenary of preventive medicine, as recorded in this scientific section of the American Medical Association, reflects the evolution of medical knowledge with regard to the etiology, prevention, and control of infectious and other preventable diseases. The historical development of this section embraces also the ever-widening concept of public health as well as the gradual integration of preventive medicine into the whole of medicine.

Environment and Infectious Disease

It is significant that at the Annual Meeting of the American Medical Association in Louisville, Ky., 1859, of the six papers listed on the general program, four dealt with epidemic diseases, namely: "Report on the Topography and Epidemic Diseases in Michigan," "Report on the Medical Topography and Epidemics in California," "Observations on some of the Physical, Chemical, Physiological, and Pathological Phenomena of Malaria Fevers," and "Report of a Special Committee on Government Meteorological Reports."

The Section on Preventive Medicine is traced to two sections which were formed in 1859. One was on Meteorology, Medical Topography, and Epidemic Diseases and the other on Medical Jurisprudence and Hygiene. These two sections were merged 12 years later under the term State Medicine, which, with slight changes, prevailed until 1900. Until 1908 it was termed the Section on Hygiene and Sanitary Science, when the name Preventive Medicine appeared for the first time. A year later, Public Health was added, and in 1922 it became the Section on Preventive and Industrial Medicine and Public Health, which continued until the single term Preventive Medicine was officially adopted in 1957.

A century ago, the medical thought concerning the causal relation between environmental factors and disease was largely influenced by the great work of Dr. Daniel Drake on "The Principal Diseases of the Interior Valley of North America." This was the first treatise on climate, atmosphere, and weather conditions affecting health since the writings of Hippocrates (460-378 B.C.). Hippocrates was also the first to use the terms "endemic" and "epidemic," and in his book on "Airs, Waters and Places" there is special reference to malarial fevers, to tertian and quartan types, and to the seasonal character of the disease.

During its first two decades the annual programs of the section included papers on "Improvement in Public Sanitation"; "Drainage and Sewage in Cities"; and quarantine regulations for measles, scarlet fever, mumps, and smallpox. Protective vaccination against smallpox became compulsory in several states, which distinctly lowered the incidence of this disease in those states.

State Boards of Health

These preventive measures became more effective with the organization of state boards of health, the first of which was established in Massachusetts in 1869, and the second in California in 1870. Thirty-two more state boards of health were formed by the turn of the century.

The American Medical Association was active in promoting health measures as far as they were then known, and continually encouraged the formation of state boards of health. When Dr. Henry I. Bowditch, founder of the first state board, was serving as President of the American Medical Association in 1877, the Association passed a resolution that an appeal be sent to the governor of each state, year after year, until a state board of health was established in that state. The names of the physicians and sanitarians contributing to the annual programs of this Section present a roster of the leading public health authorities of that period.

When, in 1872, the name of the Section was changed to State Medicine, the term was evidently interpreted as synonymous with preventive medi-

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Read before the Section on Preventive Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

cine, except that in matters of hygiene the agency of the state was extended beyond the control of the individual, first to measures of preventive medicine in general and then to curative medicine insofar as it was the duty of the state to regulate medical practice. It was further defined as the connection of the state with that branch of science which related to the prevention, cure, or alleviation of the diseases of the human body; thus it embraced not only all public sanitary measures but also the practice of medicine insofar as it was related to the state. This, no doubt, led to the association of medical licensing with state boards of health, which was continued until well into this century and is still maintained in several states. In the discussions during the next decade there was frequent reference to the regulation of medical practice by state boards of health, in the sense that such boards were created and maintained for the conservation of health and life.

Era of Bacteriology and Immunology

The last two decades of the previous century ushered in the "era of bacteriology" with the demonstration of specific bacteria and other microorganisms as etiological agents of the various infectious diseases. This led to a new concept of preventive medicine which profoundly influenced public health methods during the following decades, up to the present day.

American physicians, returning from graduate studies in European medical centers and the laboratories of Louis Pasteur in Paris and Robert Koch in Berlin, brought back the impact of the new sciences of bacteriology and immunology to every institution concerned with the training of physicians. In a farsighted forecast of this "era of bacteriology" in preventive medicine, articulated by Dr. William H. Welch of Johns Hopkins University in his "Address on State Medicine" before this Association at its Annual Meeting at Newport, R. I., June 1889, it was emphasized that the scientific basis of preventing infectious diseases was dependent on the accurate knowledge of the biological characters of the causative external agents and their methods of producing pathogenic effects.

In the continuing bacteriological and immunological studies it became evident that infectious agents were not confined to bacteria, as several infectious diseases were caused by certain species of protozoa and fungi. Later it was demonstrated that a considerable number of such diseases were of virus origin. These included variola, vaccinia, rabies, influenza, yellow fever, dengue, psittacosis, mumps, Q fever, trachoma, poliomyelitis, and the common cold.

From these newer discoveries it was revealed that, in the suppression and control of infectious diseases, several types or modes of infection were encountered. Diseases such as yellow fever, malaria, dengue, cestode infections, and, to a certain extent, bubonic plague require an intermediate host for the completion of the life cycle of the parasite before its conveyance from infected to new victims. At the opening of this century there appeared the heroic figure of Walter Reed and his yellow fever commission with their effective efforts in the control of yellow fever in Havana. Largely due to the careful experiments of Lazear, a member of the commission, before his death from self-infection, it was learned that the mosquito vector Aedes aegypti, to be infective, must sting a yellow fever victim during the first three days of illness and then, before it can transmit its deadly load to infect another person, the virus must have a chance to ripen within the mosquito's body at least 12 days. By institution of the necessary sanitary regulations to control the mosquitoes, Havana was freed from its age-old scourge. Armed with this new knowledge, Gorgas made the Panama Canal safe for the passage of the commerce of the world and the tropics habitable for the white man.

Certain diseases, such as tuberculosis, brucellosis, psittacosis, and rabies occur in animals and are directly transmitted to the human person. In a third group, purveyors of infection are recognized as flies in typhoid, the tsetse fly in trypanosomiasis, the tick in Rocky Mountain spotted fever, and the louse in Tsutsugamushi fever (scrub typhus).

A last group is composed of diseases of mankind only, in which the infection passes directly or indirectly from one human being to another, without intervention of an animal or insect host. Examples of this group are smallpox, measles, scarlet fever, diphtheria, typhoid, mumps, pulmonary tuberculosis, pneumococcic pneumonia, influenza, and poliomyelitis.

In the first three groups, the breaking of any of the links in the chain of infection will prevent transmission of the infectious disease. In the last group, since the chain consists of only two links, both human beings, the inherent difficulties of breaking this short chain of infection are much greater. It is in this group of diseases that protective vaccination or immunization has proved most effective.

Control Through Vaccination and Immunization

Of fundamental importance was the demonstration by Roux and Yersin in 1887, at the Pasteur Institute, Paris, of specific toxins produced by the Bacillus diphtheriae and the Bacillus tetani. These toxins, when injected into experimental animals, produced the systemic, organic changes of each disease; in clinical observations the causative bacilli were found only in the local lesion or portal of entry into the human body and not in the blood stream or other circulating fluids.

In Germany, Von Behring and Kitasato in 1892, produced diphtheria antitoxin by immunizing animals with increasing doses of diphtheria toxin, the blood serum of such animals having definite protective and therapeutic value in diphtheria. Tetanus antitoxin was later produced by the same method

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While the United States Army was practically free of typhoid at the time the United States entered World War I, several outbreaks did occur in the American Expeditionary Forces. According to Soper,[1] "In the 101 weeks from October 18, 1917 to September 25, 1919, there were 1529 cases of typhoid infection and 303 cases of paratyphoid with 169 deaths." Considering the large number of troops involved, nearly 2 million, and frequent changes in sanitary environment, the number of cases of infection is surprisingly small. In contrast, during the Spanish-American War more soldiers died from typhoid than from batt
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Prevention of Noninfectious Diseases

The prevention of the noninfectious diseases presents a somewhat different approach. Early in this century attention was directed to "indispensable ingredients in food," largely through the experience gained from treatment of scurvy and beriberi.

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In 1914,. Dr. Goldberger and his group established headquarters in a small hospital in Spartansburg, S. C. Extensive visits to affected areas soon convinced him that pellagra was closely related to conditions of poverty and was a nutritive disorder and not an infection. The usual diet of the pellagrin, as the victim was designated, consisted of corn muffins or other preparations of corn meal, fat meat (sowbelly), and molasses. Dr. Goldberger enlisted volunteer groups to live on this restricted diet, until the symptoms of pellagra were fully established and the diagnosis confirmed by a leading dermatologist and clinician. The volunteers were then placed on a more liberal diet of eggs, lean meat, fresh vegetables, and fruit juices, after which all the symptoms of pellagra rapidly disappeared.

All the succeeding investigations, which continued practically until Dr. Goldberger's death in 1929, confirmed the role of a deficiency factor or vitamin in the etiology of pellagra. It was referred to as vitamin "G," or as P. P., pellagra preventive, but it was not until 1937 that nicotinic acid was established as the insufficiency factor or vitamin in pellagra. Its therapeutic use together with a high-calorie diet which includes liberal amounts of milk, chicken, beef, and green vegetables has made pellagra a rare disease in the United States. Similar results have been obtained with the other diseases in which the insufficiency factor or vitamin is causative of the same.

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Control Through New Drugs and Vaccines

Schaudinn's discovery, in 1905, of the Spirochaeta pallida (Treponema pallidum) as the causative agent of syphilis, and the announcement in 1906 of the Wassermann reaction as a diagnostic test distinctly advanced the control of this infectious disease. In 1910, Ehrlich, as a result of his outstanding work in the study of the therapeutic effect of arsenic compounds in experimental syphilis, brought forth arsphenamine (Salvarsan), or 606, which, for a generation, was the most potent and widely used drug in the treatment of syphilis.

A new era in American medicine, particularly in the treatment of infectious diseases, came with the introduction of antibiotics just preceding World War II. The first group were the sulfonamide drugs, which reduced the mortality of pneumococcic pneumonia and other acute infections caused by streptococci and staphylococci to a marked degree. The second group of antibiotics, of which penicillin was the first example, were all products of lower organisms such as molds, fungi, and soil bacteria.

The story of penicillin, discovered in 1928 by Dr. Alexander Fleming, a London pathologist, constitutes another romance in medicine. He prepared the material from a common soil mold, and after it was identified by the American entomologist, Thom, as Penicillium notatum, he named the product penicillin. The clear-cut proof of its antibiotic action and clinical value with assay and unit dosage was provided by the work of Drs. Howard W. Florey and Ernest Boris Chain of Oxford. The onset of war expedited the development of penicillin, and the great need for its mass production was promptly met by enterprising drug manufacturers in the United States. It soon came into extensive use in the military hospitals of all the allied nations and may well be credited with a prominent part in winning the war.

Penicillin has had a remarkable therapeutic effect in the treatment of venereal diseases. The former methods of treatment required several years for the disappearance of symptoms, whereas now, with adequate dosage and prompt diagnosis, it is possible to render the infected person noninfective after one or two days, and eliminate all symptoms of the disease within two or three weeks. The incidence of congenital syphilis after effective prenatal treatment of the mother has been reduced to a minimum; likewise, the admission of patients with the chronic forms of the disease into mental hospitals has been lowered greatly.

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Conclusions

As we approach the close of the first century of this Section, history appears to repeat itself, in that environment is again given prominence in the causation of disease involving man's management of the health hazards connected with air pollution, stream pollution, fluoridation, and radiation.

As a result of effective control of infectious diseases and improved housing and nutrition, the human life span has been increased, so that life expectancy, estimated in 1900 at 45 years, has been increased to 70 years in 1957. At the present time about 10% of the population of the United States is 65 years or older.

The continuing increase of the aged in our population and the greater incidence of long-term or chronic illness will profoundly influence the character of medical practice and present new aspects of preventive medicine. The ultimate purpose of all present efforts in preventive medicine is the attainment and maintenance of positive health; in this direction, one can foresee that the community hospitals of tomorrow may rapidly develop into positive health centers.

A half century ago, an eminent leader in the American Medical Association voiced the spirit of this Section in the dictum "Prevention runs like a golden thread through the entire fabric of modern medicine." As one of the important scientific sections of this Association, such must ever be its destiny and high purpose.

Reference

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DIAGNOSIS AND TREATMENT OF TUMORS OF THE TESTIS

Col. John F. Patton, Lieut. Col. Clarence B. Hewitt, (MC), U. S. Army
and
Nicholas Mallis, M.D., Washington, D. C.

This paper is based on a study of 510 cases of tumor of the testis treated at the Walter Reed Army Hospital from Jan. 1, 1940, through Dec. 31, 1956. The results of therapy have been published elsewhere.[1] We are concerned here primarily with diagnosis and treatment, placing emphasis on the importance of early detection and the application of prompt and appropriate therapy.

Tumors of the testis are relatively uncommon but are among the most malignant of the body. They occur in an incidence of about 1 in 50,000 males and represent less than 1% of all malignant tumors in the male. In the age group from 20 to 35 years, however, they are one of the most common forms of malignancy encountered and reap a heavy toll of life. More than 4 of 10 of these young persons in the prime of life will die from their disease, the majority within the first two years.

Distribution of the 510 tumors into types is as follows: seminoma, 191 cases, or 37.4%; embryonal carcinoma, 157, or 30.8%; teratocarcinoma, 128, or 25.1%; teratoma, 12, or 2.4%; choriocarcinoma, 10, or 1.9%; and miscellaneous, 12, or 2.4%. Included in the miscellaneous group are the cases of interstitial cell tumor and other rare types. The average age in the

The relative value of various diagnostic findings and of various types of treatment were studied in 510 patients with testicular tumors. The average age of the patients was 27.0 years. In 26 cases the tumor appeared in a cryptorchid, and in 6 of these orchiopexy had been done. Symptoms were varied and misleading, and the onset was often insidious. Metastases to bones were exceedingly rare. The Ascheim-Zondek test, when results were positive, indicated spread and was a fairly reliable guide to prognosis. Of 389 patients, treated by various combinations of therapy and successfully followed up, 204 survived more than five years. In cases of choriocarcinoma, neither lymphadenectomy nor irradiation appeared to alter the course of the disease. In cases of seminoma, orchiectomy followed by irradiation is recommended; in cases of embryonal carcinoma and teratocarcinoma, in the absence of clinical metastases, it is recommended that orchiectomy be followed by bilateral lymphadenectomy through a transabdominal approach.

From the Urology Service, Department of Surgery, Walter Reed Army Hospital.

Read before the section on Urology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

total series was 27.9 years. Seminoma occurred in somewhat older persons with an average age of 30.7 years. Embryonal carcinoma and teratocarcinoma occurred at an average age of 26.1 and 26.6 years respectively.

The tumor appeared in a cryptorchid in 26 instances, or 5.1% (1 in 19). Six of these persons had had a previous orchiopexy. That the testis in a cryptorchid is more likely to undergo malignant degeneration than is the normal scrotal testis is well documented. Various reports give the incidence as 5 to 48 times greater. It is likewise well accepted that a successful orchiopexy does not lessen the chance of malignancy. These facts bear consideration in deciding whether or not the undescended testis in a given case should be treated by orchiopexy or the testis removed.

Five of the patients in this series developed a tumor in the opposite testis. In one patient, tumors appeared in both testes simultaneously; in the other four patients, the second tumor appeared at intervals of from 1 to 14 years. It is our opinion that persons who have had a tumor of the testis have a 40 to 50 times greater probability of developing a tumor in the remaining testis than the normal male who has never had a tumor of the testis. This is an important consideration in follow-up studies.

Classification

The classification of tumors of the testis at the Walter Reed Army Hospital follows that introduced and in use at the Armed Forces Institute of Pathology. Over 95% of the tumors fall into the following five main groups: (1) seminoma, (2) embryonal carcinoma, (3) teratocarcinoma, (4) adult teratoma, and (5) choriocarcinoma. Various combinations of these elements are not unusual. These groups may be further classified clinically according to their response to irradiation. Seminoma is sensitive to x-ray, and all the others are highly radioresistant.

Mode of Metastasis

The mode of metastasis is largely by way of the lymphatics, with the exception of choriocarcinoma, which spreads by the hematogenous route. Metastasis occurs along the lymphatic pathways which accompany the internal spermatic vessels in the cord, passing to the retroperitoneal periaortic and pericaval nodes to the level of the renal pedicles and above. As a rule lymph node involvement, when present, is limited to the affected side; however, not infrequently crossed metastasis occurs. With involvement of the above described nodes, subsequent upward and downward extension may take place. Not all tumors of the testis follow the lymphatic metastatic behavior we have outlined. The retroperitoneal periaortic and pericaval lymph nodes may be found to be entirely free of tumor, grossly and microscopically, and yet this same patient may develop mediastinal lymphatic involvement. Also the periaortic and pericaval nodes may be normal and a single external iliac node may be found with tumor. Presumably the explanation for this is that metastasis occurs as an embolic phenomenon, in which case multiple nodes are skipped. In addition, if serial sections had been made, it may have been revealed that allegedly normal nodes were not truly free of tumor. The inguinal and femoral nodes are not important from a metastatic, and therefore therapeutic standpoint, unless the scrotum or spermatic tunics are involved.

Metastasis on Admission

Seventy-one, or 13.9%, of the 510 patients had demonstrable metastasis on admission as determined by physical examination, roentgenogram, or urographic study. Forty-eight patients (9.4%) showed no clinical evidence of metastasis on admission but on attempted lymphadenectomy were found to be inoperable. If we combine these figures, we find 119 patients, or 23.3%, who had gross metastasis when first seen. The over-all mortality for the 119 patients was over 92%. With the present methods of treatment, little or no hope can be offered these unfortunate persons, except those with seminoma. These figures do not include those cases in which a lymphadenectomy was successfully accomplished but the nodes found to be positive for tumor.

TABLE 1.—*Symptoms Experienced by 491 of 510 Patients*

Symptom	Patients	
	No.	%
Swelling	365	74
Hardness or "lump"	109	22
Painless	125	25
Pain	115	23
Symptoms of spread	47	10
No symptoms (routine exam)	23	5
History of trauma	35	7

Symptoms

The symptoms associated with tumors of the testis vary considerably and are often misleading. Likewise, the onset may be so insidious that the patient is unable to state exactly when the first symptom appeared. The history is so unreliable that the diagnosis will depend entirely on the examination.

Table 1 lists the symptoms experienced by 491 of the 510 patients. The majority complained of the presence of a painless swelling or hardness of the testis. Absence of pain, however, is not a constant feature; in fact, almost an equal number had pain in varying degrees. Pain, when present, is usually not severe and is probably explained by hemorrhage within the testis. It is not unusual for the person to experience a sensation of "heaviness" in the scrotum. Ten per cent of the patients initially had symptoms indicating spread of their disease. Five per cent had no symptoms whatever, and the lesion in the testis was found on a routine examination. History of trauma, although present in 7% of the cases, is not considered an etiological factor.

Rather it is thought to be coincidental in attracting the patient's attention to an already preexisting lesion.

Table 2 shows the duration of symptoms. Sixty-five per cent of the patients had symptoms less than six months, while more than one-third had symptoms ranging from six months to more than two years. The average period for the entire series from onset of symptoms to the time of definitive therapy was four months and 28 days, approximately five months.

TABLE 2.—*Duration of Symptoms in 442 Patients**

Duration	Patients No.	Patients %
Less than 1 mo.	57	12.9
1 to 3 mo.	121	27.4
3 to 6 mo.	108	24.4
Total		64.7
6 mo. to 1 yr.	91	20.6
1 to 2 yr.	45	10.2
Over 2 yr.	20	4.5
Total		35.3

* Average duration, 4 mo. 28 days.

Diagnosis

The mortality in patients with tumors of the testis is exceedingly high. Surgery and x-ray therapy have improved the outlook for many of these unfortunate persons, but the techniques in both fields have about reached their maximum degree of refinement. The field of chemistry offers some hope but as yet is not well explored. With our present methods of treatment, the greatest hope in reducing the mortality lies in earlier diagnosis. From the figures presented in the preceding paragraph, it can readily be seen that this opportunity exists.

The testis is an external organ and, except in cryptorchism, is readily accessible for minute examination. Why, then, is there a delay in diagnosis? The patient's procrastination in seeking medical attention, of course, is a contributing factor over which we have no control. Perhaps some type of discreet educational program might be devised. In many cases the tumor may produce no symptoms or the lesion may be so small that it is not readily detected. Another source of delay is that an appreciable number are not recognized as tumor on the initial examination. The initial diagnosis in the 510 cases is shown in table. 3. An erroneous diagnosis was made in more than one-fourth of the cases, epididymitis being the most common.

Examination.—As stated previously, the diagnosis will depend, not on the history but on careful examination. Variation in the size of the scrotal contents may be noted on inspection. Palpation of the testis should always be performed bimanually. A useful rule of thumb is to always examine the opposite, supposedly normal testis, prior to palpation of the affected side. This will give the examiner a base line for comparison. The epididymis normally can be distinguished easily from the testis proper by careful palpation. The normal parenchyma of the testis is uniform in consistency and any mass or area of induration, whether sharply demarcated or ill-defined, may be considered as tumor until proved otherwise. Not infrequently the entire testis may be replaced by tumor, in which case the consistency will be firm to hard. Tenderness is usually absent but may be present to mild or moderate degree. The epididymis will be normal except in those rare instances where the tumor may have spread by direct extension. If a hydrocele is present and proper evaluation of the testis is made difficult, careful aspiration should be performed to permit more accurate palpation. The differential diagnosis includes any and all conditions to which the scrotal contents may fall heir.

The general physical examination includes palpation of the abdomen for evidence of metastasis, a careful search for lymphadenopathy, and examination of the breasts. A palpable left supraclavicular node may be the first clinical evidence of metastasis. Enlargement or tenderness of the breasts suggests hormonal activity of the tumor.

If the diagnosis remains in doubt after careful examination, the testis should be explored. This is performed through an inguinal incision, occluding the cord with a rubber-shod clamp to prevent dissemination before delivering the testis into the wound for inspection. If doubt still exists, the testis should be removed. Aspiration biopsies or open biopsies should never be performed.

Laboratory Studies.—In addition to the routine tests, the examination should include roentgenogram of the chest, excretory urograms, a quantitative Ascheim-Zondek (A-Z) test, determination of sedimentation rate, and platelet count. A skeletal survey may be made, but bone metastasis is rare.

TABLE 3.—*Initial Diagnosis Made in 510 Cases of Tumor of Testis*

Diagnosis	Patients No.	Patients %
Tumor	144	28.2
None stated	236	46.3
Erroneous diagnosis	130	25.5
Epididymitis	83	16.3
"Nothing"	19	3.7
Hematocele	2	..
Torsion	1	..
Seminal vesicle disease	1	..
Hydrocele	13	2.6
Orchitis	8	1.6
Varicocele	1	..
Cyst	1	..
Rupture	1	..

Renal or ureteral displacement and/or obstruction noted pyelographically indicates extensive lymphatic spread. Marked periaortic and pericaval lymph node involvement may exist, however, without demonstrable pyelographic evidence. The A-Z test, when results are positive, indicates spread and may be followed as a fairly accurate guide in prognosis.

Results of Therapy

Table 4 shows the five-year survival rate in the over-all series and includes the results in all types and combinations of treatment. Three hundred ninety-six patients fall in this group, and 389 of these have had adequate follow-up. It includes all patients seen from Jan. 1, 1940, through December, 1952, with follow-up extending to December, 1957. One hundred two of the 389 patients had demonstrable metastasis on admission or were found to be inoperable on attempted lymphadenectomy. An additional 51 had positive nodes on lymphadenectomy, making a total of 153, or 39.3%, who had proved spread of their disease at the time treatment was instituted. The results may be interpreted in light of these figures.

TABLE 4.—*Five-year Survival in Series of 389 Patients*

			Dead		Alive or Dead Without Tumor	
Type Tumor	Total	Alive	From Tumor	From Other Cause	Total	%
Seminoma	138	103	11	24	127	92.0
Embryonal carcinoma	125	48	70	7	55	44.0
Teratocarcinoma	103	42	57	4	46	44.7
Teratoma	8	7	1	0	7	87.5
Choriocarcinoma	8	1	7	0	1	12.5
Other	7	3	4	0	3	57.1
Total	389	204	150	35	239	61.4

Table 5 is a composite table, and the survival-rate figures for the various types of tumor are given as percentages. The number of cases for each type is not shown. All patients had been treated by orchiectomy. The majority of the 127 patients treated by irradiation had known metastasis when treatment was instituted. Of the 243 patients in the lymphadenectomy group, all but 16 received irradiation.

Treatment

It is our policy at the Walter Reed Hospital to treat tumors of the testis as surgical emergencies. Any patient with a scrotal lesion admitted to the urologic ward, regardless of the admitting diagnosis, is seen promptly by a member of the urology staff. If tumor of the testis is suspected, preliminary studies are obtained on an emergency basis and the patient taken directly to the operating room.

Orchiectomy.—Although some aspects of the treatment of tumors of the testis remain controversial, there is general agreement that a high orchiectomy should be performed through an inguinal incision and the cord severed at the level of the internal inguinal ring. We prefer to wait for a study of the permanent pathological sections rather than to proceed with lymphadenectomy, even though the gross appearance of the tumor suggests embryonal or teratocarcinoma. Multiple sections of the tumor are cut to include any unusual or hemorrhagic areas. When the type of tumor has been established, further treatment is then outlined and will depend, of course, on the presence or absence of metastasis.

The practice of extending the inguinal incision at the time of orchiectomy to palpate the retroperitoneal space for evidence of lymph node involvement is, in our opinion, unreliable and not justified. Lymph nodes may be involved but not palpable, and even if palpable they may show only reactive hyperplasia on microscopic section. Only gross involvement can be detected by blind palpation and even then will not necessarily indicate operability. This has been apparent in several recent cases. Initial palpation of the retroperitoneal nodes on opening the anterior peritoneum conveyed the impression of inoperability, but with appropriate exposure and on opening the posterior peritoneum, the mass was found to be easily removable.

Irradiation.—The value of irradiation therapy in the treatment of seminoma of the testis is well known. One can expect a cure in about 95% of patients by treatment with orchiectomy and irradiation alone, applied in a dosage of 2,000 r. Embryonal carcinoma and teratocarcinoma are highly radioresistant, and the dosage required is much greater. Although we include irradiation in the treatment of these tumors, its value is difficult to assess. In our series of 127 patients treated by orchiectomy and irradiation alone, none of those with lymph node metastasis responded to irradiation and all died within two years. The morbidity associated with the application of large dosages of x-ray may be considerable, and complications with late sequelae are not infrequent. As applied to the treatment of the radioresistant tumors, it must be considered in the realm of radical therapy.

Lymphadenectomy.—Retroperitoneal lymphadenectomy should be performed in all cases of malignant radioresistant tumors of the testis except choriocarcinoma. This applies, of course, only in the absence of clinical metastasis. In our own series it was interesting to note that, while no patient with embryonal carcinoma or teratocarcinoma who had metastasis to the retroperitoneal nodes and was treated by irradiation survived his disease, 19 of 40 patients (47.5%) with the same types of tumor and who had positive nodes on lymphadenectomy lived more than five years. Sixteen of the 19 patients were living and well from 5 to 13 years later; 3 died from other causes, and autopsy revealed no evidence of tumor. Of the 19 cases, 13 were embryonal carcinoma and 6 were teratocarcinoma.

TABLE 5.—*Five-Year Survival Rate, by Percentage, in 389 Patients*

			Lymphadenectomy		
Type	Total Group	Irradiation	Total	Pos. Node	Neg. Node
Seminoma	92.0	86.1	96.0	72.7	98.9
Embryonal carcinoma	44.0	13.0	72.3	65.0	75.6
Teratocarcinoma	44.7	17.7	60.6	30.0	73.9
Teratoma	87.5	100.0	85.7	...	85.7
Total, %	61.4	35.4	79.4	52.9	86.5
Total, No.	389	127	243	51	192

The lymphadenectomy should be bilateral in all cases, as a significant number of persons show involvement of the contralateral nodes. Bilateral dissection has been performed at Walter Reed Army Hospital since 1954. During the past two years, a transperitoneal approach has been used.[2] This has definite advantages, in our opinion, over other incisions used in the past. It provides good access to the critical area around the renal pedicles on both sides and permits adequate simultaneous bilateral dissection. One has good control of the major vessels if by chance they are injured during the procedure. The operative time is considerably reduced because of better exposure and time saved in opening and closing the wound. A total of 25 node dissections by this route have been performed to date. There have been no deaths, and the morbidity is so minimal as to justify the removal of this procedure from the realm of radicalism.

Chemotherapy.—This therapeutic field holds promise but as yet is in the early stages of development. Our experience during the past two years has shown some encouraging but, thus far, only temporary results. An active program to explore the use of the newer compounds is in effect, but no report is justified at the present time.

Suggested Treatment

On the basis of our present knowledge and experience, the current policy for treatment of testis tumors at the Walter Reed Army Hospital is as follows.

Seminoma.—In patients with seminoma, orchiectomy is followed by irradiation to the abdominal lymphatic chain. This consists of giving a total tumor dose of 2,000 r through opposing portals for an average period of 28 days. If metastases are clinically present in the abdomen, mediastinum, and/or the clavicular areas, irradiation therapy is then directed to the entire lymphatic chain, giving a total tumor dose of 2,000 r to each area. This can usually be given in an average period of 50 days. If there are metastases to the lung, these areas are included in the radiation field. Lymphadenectomy in patients with seminoma is unnecessary. If the microscopic sections, however, show anaplasia, or the diagnosis of "pure" seminoma is in doubt, lymphadenectomy is performed prior to irradiation.

Embryonal Carcinoma and Teratocarcinoma.—In patients with embryonal carcinoma and teratocarcinoma, in the absence of clinical metastasis, orchiectomy is followed by bilateral lymphadenectomy performed through a transperitoneal approach. If the nodes removed are negative pathologically, no further therapy, such as irradiation, is given. If any of the nodes removed reveal metastasis, or if at the time of surgery the patient was found to be inoperable and only a biopsy specimen could be obtained, postoperative irradiation is applied to the entire lymphatic chain, including the left supraclavicular area, mediastinum, and abdomen. A tumor dose of 4,000 r is delivered to each of these areas over an average period of 110 days, beginning with the upper abdominal portal. An exposure of 4,000 r is considered the upper limit of safety. All irradiation is given by the million-volt therapy equipment. If clinical evidence of metastasis is present prior to treatment, orchiectomy is followed by irradiation applied to the entire lymphatic chain. Treatment in these advanced cases, or in those patients who return with metastasis, unfortunately may be limited to palliative measures. These include nitrogen mustard therapy with ACTH, use of a cytotoxin, castration with or without supplemental use of diethylstilbestrol (Stilbestrol), and local irradiation.

Teratoma in the Adult.—Treatment is the same for teratoma as for teratocarcinoma. Lymphadenectomy is considered justified because of the minimal surgical risk and the incidence of metastasis by elements other than teratoma.

Choriocarcinoma.—Patients with choriocarcinoma are treated by orchiectomy only. If metastases are present, lymphadenectomy and/or irradiation will not alter the course of the disease. Chemotherapy offers the only hope in patients with this type of tumor.

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STRIAE GRAVIDARUM.—Striae gravidarum should no longer be considered as "stretch marks." There is strong evidence that they are closely related to adrenal cortical hyperactivity. In a study of 116 primigravid pregnancies it was shown that: the formation of striae gravidarum does not depend directly upon skin stretching; this only influences the production of striae in the presence of a "striae factor." There is a close relation between lowered glucose tolerance in late pregnancy and the development of striae gravidarum. There is a close relation between acne, a sign of adrenal cortical hyperactivity, and breast striae, particularly as regards time of onset. Several other clinical findings all lend support to an association between striae gravidarum and adrenal cortical hyperactivity.—L. O. S. Poidevin, Striae Gravidarum: Their Relation to Adrenal Cortical Hyperfunction, *Lancet*, Sept. 26, 1959.

METABOLIC CAUSES OF RENAL STONES IN CHILDREN

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A 7-year-old girl had had abdominal pain, nausea, vomiting, and fever since the age of 2 years. When she was 3 years old she passed the first renal stone. During the next three years preceding hospitalization she passed stones on the average of one every one or two weeks. These episodes were usually accompanied by high fever, abdominal pain, and nausea. The cause was ultimately found to be a primary hyperoxaluria. A review of the literature shows that about half of the reported cases of urolithiasis in children have been ascribed to causes unknown, with only 10% definitely traced to metabolic disease. This case suggests that more detailed study might often lead to recognition of the underlying metabolic aberration and that diagnostic laboratory procedures not generally available may sometimes be necessary if the patient is to be spared the consequences of misdirected treatment.

Renal stones and nephrocalcinosis are rare conditions in childhood. In 1957 Myers[1] reviewed the records for the previous 10 years of the Hospital for Sick Children and found an incidence per 1,000 admissions of about one child with urolithiasis. About 30% were associated with renal anomalies; 6% resulted from other recognizable causes such as recumbency, foreign body, and neurogenic bladder; and 10% were of metabolic origin. In 54% the etiology could not be determined.

The discovery of a renal stone in a child always should lead to a thorough investigation of the genitourinary tract. In the recumbent or paralyzed child stone formation is to be anticipated and therefore must be guarded against by the liberal intake of fluids as well as early mobilization of the patient. Such general principles have been stated many times and must be followed. It should also be remembered that occasionally burns, pyloric stenosis, leukemia, heavy metal poisoning, vitamin-D intoxication, and sarcoidosis may lead to renal calcification in children. If there is an awareness of these differential possibilities, the diagnosis of any of these disorders is seldom difficult.

In contrast, the discovery of metabolic errors depends on time-consuming methods of clinical study as well as performance of laboratory techniques which unfortunately are not generally available. This phase of the problem is emphasized here in the belief that diligent search will reveal that metabolic disease is a more important etiological factor than present statistics indicate. With this viewpoint in mind the large group of patients with stones for which no cause can be found offers an intriguing challenge.

Causes

In this discussion, the causes of kidney stones and calcification have been divided into three groups as follows: endocrine causes, including hyperparathyroidism and adrenal cortical hyperfunction, with Cushing's syndrome; renal tubular disorders, including renal tubular acidosis, cystinuria, xanthinuria, and glycinuria; and generalized metabolic disorders, including idiopathic hypercalcemia and primary hyperoxaluria.

Endocrine Causes.—At the mention of metabolic causes of renal stones, most of us immediately think of the possibility of hyperparathyroidism. Unfortunately, after this diagnosis has been excluded, too often our thoughts are limited with regard to further investigation of metabolic errors. Certainly in all children suffering from unexplained urolithiasis it is worth while to rule out hyperparathyroidism, inasmuch as this is a curable disease in patients in whom extensive renal damage has not occurred. In adult patients parathyroid adenoma accounts for 5% of all renal stones. However, in children cases of renal stone associated with proved parathyroid adenoma have only rarely been reported.[2] This diagnosis may be made more frequently by the use of such new methods of study as determinations of calcium tolerance, phosphate reabsorption, and phosphate deprivation. Secondary hyperparathyroidism seldom causes calcium deposition in the kidney, although it may cause ectopic calcification in the subcutaneous tissues, in the arteries, and about the joints.

Another endocrine disorder which may be accompanied by renal calculi is adrenal cortical hyperfunction, with Cushing's syndrome. In this condition excessive steroid production leads to osteoporosis and increased urinary calcium excretion, with resulting stone formation. The complication of renal stones, therefore, should be anticipated in any child receiving large amounts of exogenous steroids therapeutically.

Renal Tubular Disorders.—Renal tubular acidosis is frequently, although not invariably, associated with nephrocalcinosis. This disorder is recognized clinically by the paradoxical findings of a sustained

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metabolic acidosis accompanied by an alkaline or only slightly acid urine. The fundamental abnormality seems to be an inability to form an acid urine with the excessive urinary loss of the basic cations of K^+, Ca^{++}, Mg^{++}, and Na^+. Apparently the high urinary excretion of calcium together with the alkalinity of the urine leads to the precipitation of calcium salts in the medullary portion of the kidney. Loss of cations (K^+, Ca^{++}, and Mg^{++}) also explains other manifestations which may occur such as tetany and periodic weakness or paralysis. Decreased phosphate reabsorption is a factor in the vitamin D–resistant, hypophosphatemic rickets frequently found in older children with renal tubular acidosis.

Clinically there appear to be two distinct types of this disorder. First, there is the renal tubular acidosis of infancy described by Lightwood and others.[4] Patients with this condition are usually infants under 18 months of age and exhibit vomiting, dehydration, weakness, constipation, and failure to thrive. In this age group a frequent finding on roentgenographic examination is a faint ground-glass appearance of the medullary region of the kidney. Actual stone formation does not occur. If these infants are treated promptly and adequately with alkalinizing solutions, they usually recover without sequelae.[5] Without therapy, however, severe acidosis and death may ensue.

The second type of renal tubular acidosis is usually seen in the older infant or child.[6] This tends to be a chronic disease requiring treatment for the rest of the patient's life. These children may also show vomiting, dehydration, weakness, constipation, and failure to grow. They frequently have the manifestations of vitamin D–resistant rickets which, without treatment, progress to severe skeletal deformity. Stone formation is common and may be of diagnostic importance in differentiating this condition from Fanconi's syndrome, in which urolithiasis is seldom seen.[7]

Treatment consists of oral administration of alkalinizing salts. Mixtures containing sodium citrate, potassium citrate, and citric acid are most commonly used. Vitamin D in moderately large amounts may also be given if rickets is present. Complete remission of all symptoms during therapy is possible unless renal damage has occurred. Renal calcification is usually not improved, although it does not progress after the acidosis is controlled. It is apparent, therefore, that early diagnosis and adequate treatment are of the utmost importance.

Cystinuria is one of the most common of all hereditary tubular disorders. About one person in 600 has this abnormality, which results in the defective reabsorption of cystine, lysine, arginine, and ornithine.[8] However, the incidence of actual formation of urinary tract stones in persons with this disorder is estimated to be only 1 in 10,000 or 20,000 of the population. Stone formation results from the excessive excretion of cystine, which is insoluble at the normal pH of the urine. Unless this complication occurs, the person is asymptomatic. There are apparently two hereditary patterns for this disorder, one involving a simple recessive gene and the other an incompletely recessive one.[9] The dignosis of cystinuria depends on identification by chromatography of the involved amino acids in the urine. Cystine stones are roentgenographically visible. Administration of alkaline salts reduces stone formation, since cystine is more soluble at an increased pH. Adequate fluid intake is also important in the prevention of cystine precipitation. Recently Smith and co-workers[10] recommended a diet low in methionine in patients who fail to respond to other measures.

Simple xanthinuria in a 4-year-old child, with resulting formation of nonradiopaque xanthine stones, has been described by Dent and Philpot.[11] This appeared to be caused by a single tubular defect involving the reabsorption of xanthine. Clinical recognition of the syndrome depends on the finding of low plasma and urine uric acid levels, with large amounts of xanthine, in the urine of a child with symptoms of urolithiasis.

Glycinuria is another tubular disorder in which there is a failure of reabsorption of a single amino acid, glycine.[12] This appears to be a hereditary disease with a dominant pattern of inheritance. Calculus formation beginning in childhood is the only clinical manifestation of the condition. The stones are composed of oxalate.

Generalized Metabolic Disorders.—I shall now consider the general metabolic disturbances which cause renal calcification. An entity which is gradually receiving more attention in the United States[13] is idiopathic hypercalcemia of infancy. The onset usually occurs between the 2nd and 8th months of life. The clinical features, like those of renal tubular acidosis, are failure to thrive, hypotonia, vomiting, loss of appetite, constipation, and irritability. Severely affected infants often show mental retardation, typical facies, hypertension, cardiac murmurs, and craniosynostosis. Osteosclerosis of the base of the skull as well as the vertebrae and long bones may be present. Laboratory studies show increased serum calcium, blood urea nitrogen, and phosphorus levels and a decreased alkaline phosphatase level. The serum cholesterol level may be high. Urinary excretion of calcium is only moderately increased. In the more benign cases recovery may be seen within several weeks after initiation of therapy. In the severe form the course is more protracted and usually ends fatally. The survivors may be both physically and mentally retarded. Nephrocalcinosis has occurred in 20% of the reported cases.[13b] Treatment consists principally of the limitation of calcium and vitamin D in the diet and the administration of adrenal corticosteroids. Although the underlying pathogenesis is not understood, the most attractive etiological possibilities are an increased sensitivity to vitamin D or an error in the vitamin D–like sterol or cholesterol synthesis, with the production of a substance which is not vitamin D itself but resembles it chemically and physiologically.[14]

Primary hyperoxaluria is yet another inborn error of metabolism which has been thought to be rare but is likely to prove surprisingly prevalent. The etiology is thought to be an aberration in the metabolism of glycine[15] which results in the excretion of large amounts of oxalate. The true incidence of this disorder will be determined only when urinary oxalate determinations are more generally available. This is believed to be a familial disease and is characterized by renal calculus formation, nephrocalcinosis, and deposition of calcium oxalate in extrarenal tissues. The usual course is one of passage of many stones, recurrent pyelonephritis with eventual renal failure, hypertension, and death in childhood or early adulthood. There is no definitive treatment.

Report of a Case

A 7-year-old girl had had abdominal pain, nausea, vomiting, and fever since the age of 2 years. When she was 3 years of age she passed the first pea-sized renal stone. During the next three years preceding hospitalization she passed stones on the average of one every one to two weeks. These episodes were usually accompanied by high fever, abdominal pain, and nausea. She was treated for many months with chloramphenicol for a persistent urinary tract infection. The child's increasing irritability and easy fatigability prompted her referral on April 16, 1957, to the University of Texas hospitals for study.

Family history revealed that the patient's maternal grandfather had had some kind of kidney disease as a child but was no longer symptomatic. Much later it was learned that her father had had recurrent hematuria. Survey of other members of the family revealed no evidence of renal stones. The patient's physical appearance was that of a child somewhat small for her age, being in the 25th percentile for height and weight. No other abnormalities were noted. However, roentgenograms revealed multiple bilateral urolithiasis.

Extensive investigation at that time, including complete urologic study, roentgenograms of the bones, slit-light examination of the eyes, chemical analysis of the stone, phosphate reabsorption studies, repeated determinations of the serum and urine electrolyte, calcium, phosphate, and uric acid levels, and pH and paper chromatography of the urine, failed to disclose any etiological basis for the extensive stone formation. During this hospital stay she underwent several procedures for dilation of the ureter and removal of stones. Six months later she was readmitted, and all studies were repeated. Still no cause for the stones could be found.

It was not until her third hospital admission one year later that the patient's urinary excretion of oxalate was determined and the diagnosis was made. Exceptionally high values, between 90 and 200 mg. per 24 hours, were found, thus establishing the diagnosis of primary hyperoxaluria. Since that time the patient has been seen frequently. She has been treated vigorously for an infection with Proteus vulgaris which seems to have cleared up only recently. She has also received large amounts of pyridoxine, folic acid, and vitamin B_{12}, since these vitamins are known to be important in the serine-glycine transformations and C_1 fragment utilization. Subjectively, she is much improved, and she has passed fewer stones, but roentgenograms show no change and her oxalate excretion remains relatively high.

The child's history illustrates how the omission of a single laboratory determination may cause a metabolic defect to remain undiagnosed in spite of extensive investigation. It also shows the remarkable clinical improvement which may follow the institution of such general therapeutic measures as control of infection and correction of inadequate fluid and dietary intake, even when no specific treatment is available.

Summary

There are numerous causes of renal stones and calcifications in children. To determine the pathogenesis in a given instance requires close cooperation between pediatrician and urologist in a thorough study of the patient. This may necessitate the carrying out of many special laboratory procedures, some of which are not generally available.

At present most kidney stones in children appear to have an unexplained etiology. However, in view of the increasing knowledge of a number of metabolic disorders which may be responsible for stone formation, it is apparent that continued investigation will bring to light additional instances of urolithiasis in children due to aberrations in metabolism. A child with marked urolithiasis was found to have primary hyperoxaluria, after extensive clinical and laboratory studies.

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PERIURETERAL FASCITIS

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Periureteral fascitis is generally part of a more extensive process, in which retroperitoneal inflammation leads to proliferation of connective tissue to form dense fibrous plaques. The lesion sometimes envelops a ureter; when this happens on both sides the patient experiences the insidious onset of a number of symptoms. These include low back pain, abdominal discomfort, nausea, and vomiting, the only distinctive one being anuria. In the case here described, a man aged 46 had vague pain six months before the anuria appeared. Surgery became necessary, first on the left to establish a nephrostomy and intubate the ureter and later on the other side to free the right ureter from its bed. The patient recovered and was symptom-free five years later.

Bilateral obstruction of the ureters as a result of extrinsic compression and envelopment by a retroperitoneal inflammatory process was initially described by Ormond[1] in 1948. He reported two cases in which the presenting clinical picture was complete anuria preceded by a history of indefinite back pain, fatigue, and reduced efficiency. Since this original report 23 cases have been described in the literature. This presentation is prompted by our experience with a patient whose case was originally discussed before the New England Urological Association in 1954 and whose progress has been followed regularly up to the present time. It is worthy of note that we have since encountered three additional patients with relatively similar disease. At the time of our original report only eight comparable cases had been reviewed, which suggests that we were dealing either with a new disease entity or with a lesion previously existing but unrecognized. The former would appear more logical in view of the careful and competent investigation of suspected or actual urologic disease during the past years.

We believe that the disease has definitely been established as a clinical urologic entity. It is insidious in its onset, with vague clinical manifestations, rarely if ever diagnosed in its early stages, and never recognized until the effects of ureteral obstruction and its attendant hydroureter, hydronephrosis, and renal damage have taken place. Urinary symptoms are conspicuous by their absence, with the result that the general practitioner, the internist, or the orthopedic surgeon rather than the urologist is initially consulted. The condition has been variously referred to as periureteritis plastica, idiopathic retroperitoneal fibrosis, nonspecific retroperitoneal inflammation, periureteric fibrosis, and perirenal fascitis. There has been a paucity of factual information about the etiology and pathogenesis. It is significant, however, that no case was recorded in the preantibiotic era. An allergic factor has also been postulated. Are we dealing with abortive perirenal suppuration? It is generally agreed that the

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basic histopathological processes are those of fibrosis, with variable degrees of inflammatory reaction from the acute phase with proliferation of connective tissue to dense fibrous plaques; that is, various stages in the healing of an inflammatory process. The lesion may envelop and involve a variable segment of the ureter, or a diffuse type of inflammatory reaction, extending from the perirenal spaces down along both ureters, aorta, and vena cava to the brim of the pelvis, may be present.

Hutch and co-workers[2] emphasized striking differences between the patient with so-called periureteritis plastica described by Vest and Barclare[3] and the other 23 patients, who, they concluded, presented basic similar disease, although varying in degree and extent. They attached the term "perirenal fascitis" to the process. In their outstanding contribution Hutch and co-workers postulated that the fibrous plaque demonstrated in these patients is a chronic inflammation of Gerota's fascia and the fat contained within it and that the growth and extent of the process is limited by the boundaries of this fascia. They believed that periureteritis plastica is a separate entity, because in the reported cases the lesions were unilateral, the distal ureter below the pelvic brim was involved, and the enveloped portion was in normal anatomic position rather than displaced medially toward the vertebral bodies, vena cava, and aorta, as was noted in the other group.

The predominant symptom of the disease is anuria. This developed in nine of the previously reported patients and it is logical to conclude that, in view of the existing disease, complete anuria would be inevitable in most cases, if intervention had not been effected. Low back pain, abdominal discomfort, nausea and vomiting, edema, testicular pain, and easy fatigue have also been observed. As previously stated, specific urinary symptoms have not been significant. An important diagnostic clue is medial deviation of the ureteral segment enveloped by the fibrous plaque, demonstrable by pyelography. The ureter below appears normal and there may be variable degrees of dilatation above the involved portion. Cystoscopy, with ureteral instrumentation and retrograde pyelography, is practically indispensable, although intravenous studies may occasionally lead to a presumptive diagnosis. In view of the apparently increased incidence of the disease urologists are becoming more conscious of the possibility of its presence, with the result that earlier recognition is now taking place. Recently, however, we made a preoperative diagnosis of the lesion and encountered instead an inoperable carcinoma of the ureter, with extensive retroperitoneal spread. Other diseases which may simulate the condition are nonopaque calculus, retroperitoneal sarcoma or lymphoma, carcinoma of the pancreas or ovary, and metastatic malignant disease.

The management of the disease is directed to the establishment of uninterrupted urinary drainage; eradication of infection, when demonstrated; and maintenance of renal integrity. Ureteral catheterization should be employed but in most instances has only temporary value, although Talbot and Mahoney[4] attributed permanent efficacy to this maneuver in their case. We believe it is reasonable to state that, once the diagnosis has been established or even presumed, surgical exploration is warranted, since when one is dealing with a fibrous mass enveloping and compressing the ureter it would be most unusual to anticipate permanent results from mere medical or instrumental measures. Conservatism can be overdone and may lead to irreversible ureteral damage, spelling defeat for both patient and surgeon. The transperitoneal approach has been employed to advantage in bilateral lesions, since it allows a direct attack on both ureters and the plaques of fibrous tissue; but in general the standard flank approach is adequate and facilitates nephrostomy drainage, when this is indicated. Simple lysis of the ureter may suffice, although the status of the ureter may warrant segmental resection with reanastomosis, intubation, and associated nephrostomy, and in the late stages of the disease the sacrifice of the kidney may be necessary.

Report of a Case

A 46-year-old man was admitted to the Carney Hospital with complete anuria of at least 24 hours' duration. He stated that for approximately six months he had experienced vague indefinite left flank pain, intermittent in character and unassociated with any other symptoms, until one month prior to admission, when it became severe and was accompanied by nausea and vomiting. The pain subsided, but the nausea persisted. He began to tire easily. There were no urinary symptoms. An intravenous pyelogram was done at a local hospital and revealed a mild bilateral hydronephrosis, with dilatation of the proximal third of the right ureter. The left ureter was not visualized. There was severe bilateral pain, which persisted with variable severity up to day of admission. He had not voided for over 24 hours. He had had medication with sulfonamides for three days prior to admission. The patient's history was essentially negative. Physical examination revealed a well-developed, well-nourished man, with moderate pallor, afebrile, and with normal heart and lungs. His blood pressure was 144/90 mm. Hg, the kidney regions were normal, edema was not present, the external genitals were normal, and on rectal examination the prostate was not remarkable. On admission he was catheterized and less than 20 cc. of urine was obtained.

Significant laboratory findings included concentrated urine, with a large trace of albumin and no sugar. There were many red and a few white blood cells in the sediment. The nonprotein nitrogen level was 82 mg.%, sedimentation rate (Westergren, corrected) 52 mm. in one hour, white blood cell count 8,400 per cubic millimeter, with a normal differential count, hematocrit value 34%, and electrocardiogram normal.

The patient was treated as having a case of acute uremia. He excreted no urine for the first four hospital days but voided 1,800 cc. on the fifth day. He was anuric thereafter until the 10th day after admission, when diuresis took place; he continued to void thereafter and on the 16th day excreted 4,900 cc. During the period of anuria the nonprotein nitrogen level rose to 125 mg.%. A urologic consultation was obtained, but in view of increasing diuresis investigation was postponed. He was discharged 19 days after admission with an appointment to be readmitted for urologic evaluation.

On readmission two weeks later the patient's nonprotein nitrogen level was 33 mg.%. Intravenous urography delineated no excretion from the left urinary tract. There was dilatation of the upper third of the ureter, the pelvis, and the calices. Cystoscopy showed the bladder to be normal. A 5 French catheter was passed readily along the right ureter, but 4, 5, and 6 French catheters encountered impassable obstruction 14 cm. above the left orifice. A plain roentgenogram of the kidney, ureter, and bladder was normal. A right ureteropyelogram made with the catheter withdrawn showed the middle third of the ureter to be markedly displaced medially, with angulation. The upper third of the ureter, pelvis, and calices were dilated. The left ureteropyelogram was unsatisfactory; there was no medium above the area of obstruction, with some medium trapped at this point and some medial deviation.

In view of these findings exploration of the left ureter was planned. On April 22, 1954, exploration of the left ureter was carried out through a left lumbar incision extended anteriorly and inferiorly. The upper third of the ureter and the renal pelvis were considerably dilated, without adherence. The ureter was followed distally to its middle third where it was angulated, with the ureter at this point deeply imbedded in firm, almost calcified, fibrous tissue for a distance of approximately 5 cm., below which the ureter felt normal. After careful dissection the ureter was freed from its fibrous bed, but it was narrowed and "pipe-stem" in consistency. A representative specimen was obtained for the purpose of biopsy. In view of the status of the right upper urinary tract, which presumably was involved with similar disease, a nephrectomy was not justified; excision of the strictured area, with end-to-end anastomosis, was not technically feasible; and so nephrostomy with ureteral intubation was decided on. The kidney was freed from its bed and a nephrostomy tube was inserted into the pelvis, accompanied by a no. 10 self-retaining catheter, which was passed along and through the incised, widely opened, strictured segment into the normal lower ureter. Intubation without ureteral closure was deemed the best solution. The patient's postoperative course was uneventful.

Pathological findings included fatty and fibrous connective tissue containing blood vessels, some of which showed calcification of their media. There was perivascular infiltration of fatty tissue by lymphocytes and monocytes and increased collagenous tissue. The findings were those of a nonspecific chronic inflammatory reaction of fatty and fibrous tissue with fibrosis and scarring.

On May 15 exploration of the right ureter was performed and similar findings were noted, but, after the ureter was freed from its bed, there was satisfactory drainage and its general appearance showed no particular abnormality. No further surgery was carried out, although transplantation of the involved portion of the ureter through the peritoneum was attempted. We were not satisfied with its practicability, however. The left nephrostomy tube and ureteral catheter were removed six weeks after operation, and the patient was discharged two days later. The incision was dry and healed. The patient has been evaluated at regular intervals since his discharge from the hospital. Bilateral ureteral dilatation has been carried out with 6 and 7 French catheters, without any semblance of obstruction. He has been free of symptoms. The urine and the nonprotein nitrogen level have been normal, and retrograde pyelograms have revealed a relatively normal upper urinary tract, approximately five years after recognition of the disease and its surgical treatment.

We are in complete agreement with Hutch and co-workers about the part Gerota's fascia takes in this disease. However, in the patient under discussion we are employing the term "periureteral fascitis," since there was no demonstrable evidence of involvement of the perirenal tissues and this term most accurately describes the lesion.

Summary

The progress of a patient with bilateral periureteral fascitis was followed for five years after recognition and treatment of the disease. This disease must be considered in a patient with acute anuria without well-established etiology. Although it is fundamentally a urologic disease, the medical profession in general should be alerted to its increased incidence.

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The pathological findings were reported by M. Shapiro.

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"PSEUDO-INFARCTION" PHENOMENON OF ACUTE PERICARDITIS

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The differential diagnosis between acute myocardial infarction and acute pericarditis is important because it markedly affects treatment and prognosis. In occasional instances the acute inflammatory reaction of pericarditis is localized to a relatively small area of ventricular wall and the electrocardiogram resembles that of myocardial infarction. The term "pseudo-infarction" phenomenon is suggested for this condition. It may mimic myocardial infarction so closely that the latter is distinguished with certainty only by the appearance of pathological Q waves. In the present case of a 9-year-old boy admitted to a hospital with the chief complaint of moderately severe precordial pain of four days' duration, the signs and symptoms suggested myocardial infarction, but the final diagnosis was acute idiopathic pericarditis.

Since the classic paper of Barnes and Burchell [1] on acute pericarditis in 1942, there have been numerous articles on the subject.[2] Its electrocardiographic differentiation from acute myocardial infarction has been repeatedly described.[3] However, it occasionally presents an electrocardiographic picture which may closely simulate myocardial infarction. The purpose of this paper is to describe this phenomenon and to present an illustrative case.

The "pseudo-infarction" phenomenon may be defined as a group of electrocardiographic signs which are caused by localized acute pericarditis and characterized by localized S-T segment elevation and reciprocal S-T segment depression; they may show major QRS changes but never Q waves. The pseudo-infarction phenomenon is caused by an inflammatory reaction which for some reason is more focal than diffuse. Additional electrocardiographic findings which may be present are found in the table.

Report of a Case

History.—A 9-year-old boy was admitted to St. Joseph's Hospital on April 9, 1957, with a chief complaint of precordial pain of four days' duration. The pain was moderately severe and related to respiration. He had been well until two weeks previously, when he had had an infection of the upper part of the respiratory tract. Since that time there had been malaise and intermittent fever.

Electrocardiographic Differential Diagnosis of Acute Pericarditis and Acute Myocardial Infarction

Electrocardiographic Characteristics	Generalized Acute Pericarditis	Acute Transmural Myocardial Infarction	Localized Acute Pericarditis
S-T segment elevation	Generalized	Localized	Localized
Reciprocal S-T segment depression	Absent	Present	Present
QRS changes	Minor or none	Major; usually with Q waves	May be major, but no Q waves
Shape of S-T segment	Concave upward	Convex upward	Convex or concave upward
T wave inversion	Usually after S-T segment returns to base line	Before S-T segment returns to base line	Before or after S-T segment returns to base line

Clinical Examination.—Temperature was 102 F (38.9 C), rectally, pulse rate 120 per minute, respirations 28 per minute, blood pressure 104/60 mm. Hg. There were no other positive physical observations except for slight enlargement of the right anterior cervical lymph nodes. The pharynx was normal, and there were no abnormal cardiac findings except for sinus tachycardia.

Laboratory Data.—Throat culture, on admission, revealed beta hemolytic streptococci, type not determined. The results of urinalysis were negative. The hemogram was as follows: Westergren sedimentation rate 84 mm. per hour; red blood cell count 4,100,000 per cubic millimeter; hemoglobin level 13.1 Gm. per 100 cc.; white blood cell count 19,200 per cubic millimeter, with a differential count of 72% polymorphonuclear leukocytes and 18% lymphocytes. Heterophil agglutination, on April 9, 1957, was positive in a dilution of 1:14. Antistreptolysin titer was 1,250 Todd units on April 10, 1957. Results of skin tests were negative for coccidioidomycosis, tuberculosis, and brucellosis. Serum glutamic oxalacetic transaminase activity was 16 units on April 12, 1957, and the test was not repeated. The series of electrocardiograms and roentgenograms are seen in figures 1 and 2.

Course in Hospital.—Therapy consisted of bed rest, administration of penicillin, and symptomatic measures. The patient became afebrile after three hospital days and the blood sedimentation rate gradually returned to normal. The antistreptolysin titer rose to 2,500 Todd units on April 25, 1957. A loud pericardial friction rub was heard on April 12, 1957, and continued to be heard daily until May 2, 1957, a total of three weeks. Maximal intensity of the rub was at the fourth left intercostal space adjacent to the sternum. At no time was a significant murmur or gallop rhythm heard. Although

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rheumatic fever was considered an etiological possibility, Jones' criteria (American Heart Association modification) were not even loosely fulfilled. Final diagnosis was acute idiopathic pericarditis.

On follow-up examination on April 10, 1958, exactly one year from the date of his first electrocardiogram, the child had been completely asymptomatic during the intervening year and no murmurs were heard. In addition to the standard leads recorded through the V_8 position, exploratory leads were recorded at V_4 through V_8, one, two, and three interspaces above and one interspace below the standard leads. There were no findings to suggest residual myocardial damage (fig. 1).

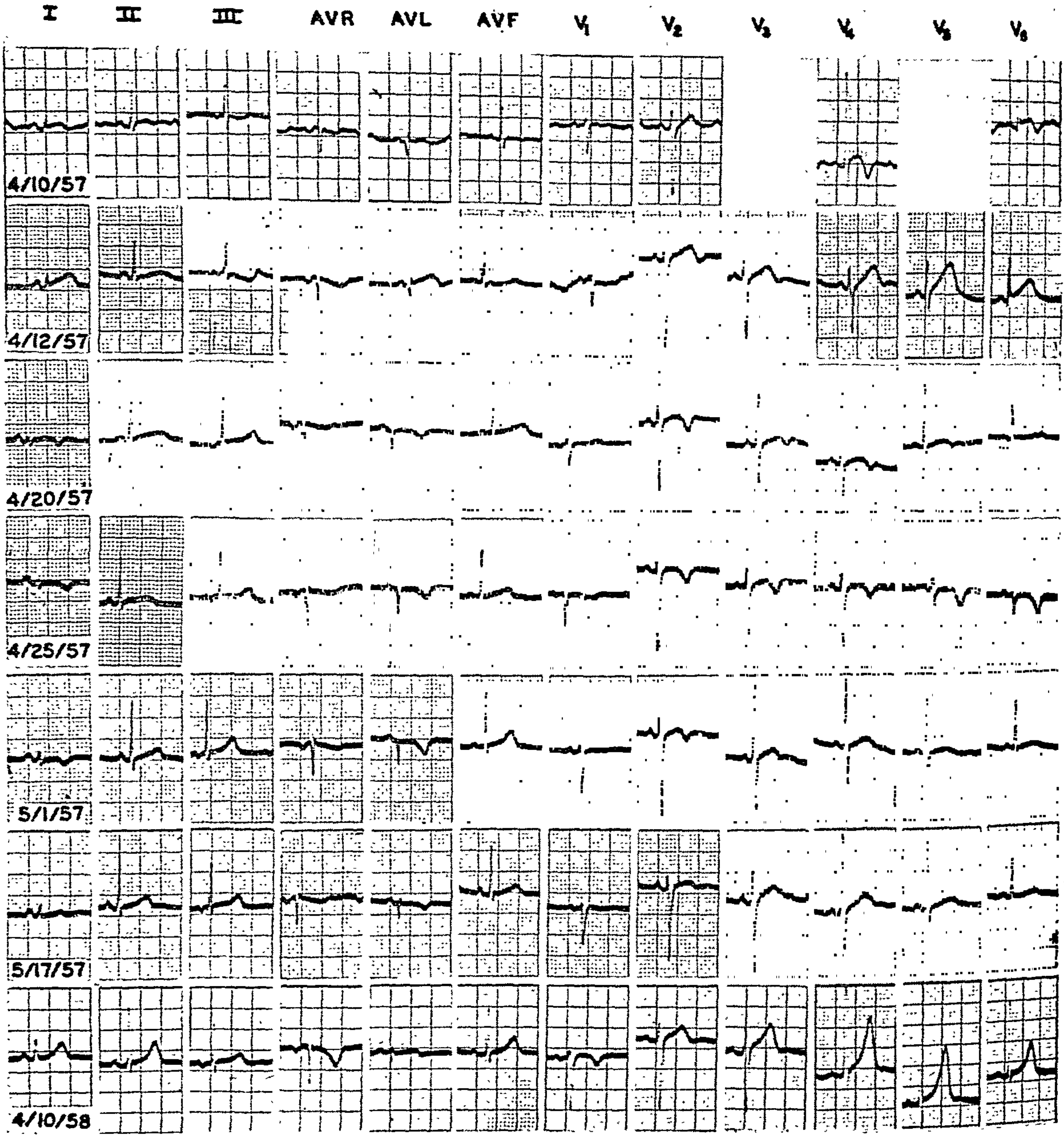

Fig. 1.—Electrocardiographic series illustrating "pseudo-infarction" phenomenon of acute pericarditis. 4/10/57: Elevation of S-T segment in lead I, with reciprocal depression in lead III; upward convexity of S-T segment with terminal inversion of T wave in leads V_4 and V_6; leads V_3 and V_5 not recorded. 4/12/57: T waves in leads I, V_4 through V_6 markedly upright; reciprocal depression of S-T segment in leads III and aVF more pronounced; lead II, which typically shows major S-T segment elevation in generalized pericarditis, essentially unaffected. 4/20/57: S-T segment returned to base line; T wave inverted in leads I, aVL, and leads V_2 through V_5. 4/25/57: Marked loss of R wave, particularly in leads I, V_4, V_5, and V_6. 5/1/57: Rapid return toward normal. 5/17/57: Almost complete return to normal. 4/10/58: Normal; compare QRS in lead I with that recorded 4/25/57; changes confirm changes in lateral chest leads. Series suggests localized process.

Comment

Although localized pericarditis has been described very adequately experimentally,[4] it has received practically no attention in the clinical literature. In fact, reports continue to appear in which the authors state that reciprocal S-T segment depression never occurs in acute pericarditis. No sharp distinction between generalized and localized pericarditis was made in the original paper of Barnes and Burchell,[1] but we noted that 1 of their 14 cases (case 3) was similar to ours, although the changes were less dramatic. It is interesting to note that films *A* and *B* (fig. 2) suggest a diffuse pericardial effusion, whereas the electrocardiograms recorded on the same dates suggest a lesion localized to the anterolateral wall of the left ventricle (fig. 1).

Obviously, in a 9-year-old boy, the clinical differential diagnosis of acute pericarditis and acute myocardial infarction is rather easy, but this is not always true in an adult. As figure 1 shows, in an adult the electrocardiographic tracings from April 10 through April 25, 1957, could easily be mistakenly interpreted as "compatible with anterolateral myocardial infarction." Thus it is apparent that pericarditis cannot be easily excluded in an acute illness that clinically suggests myocardial infarction unless pathological Q waves are present. This is especially true now that Kalmansohn and Kalmansohn[5] have shown that acute pericarditis may elevate the level of serum glutamic oxalacetic transaminase. False diagnosis of myocardial infarction may result in anticoagulant therapy, which has been held by some[6] to be definitely contraindicated in acute pericarditis. Even more important may be the mental trauma suffered by a patient who carries the stigma of a deadly chronic disease when his actual illness is benign and transient. In the later stages, electrocardiographic recovery will usually be so rapid that it should be obvious that infarction has not occurred.

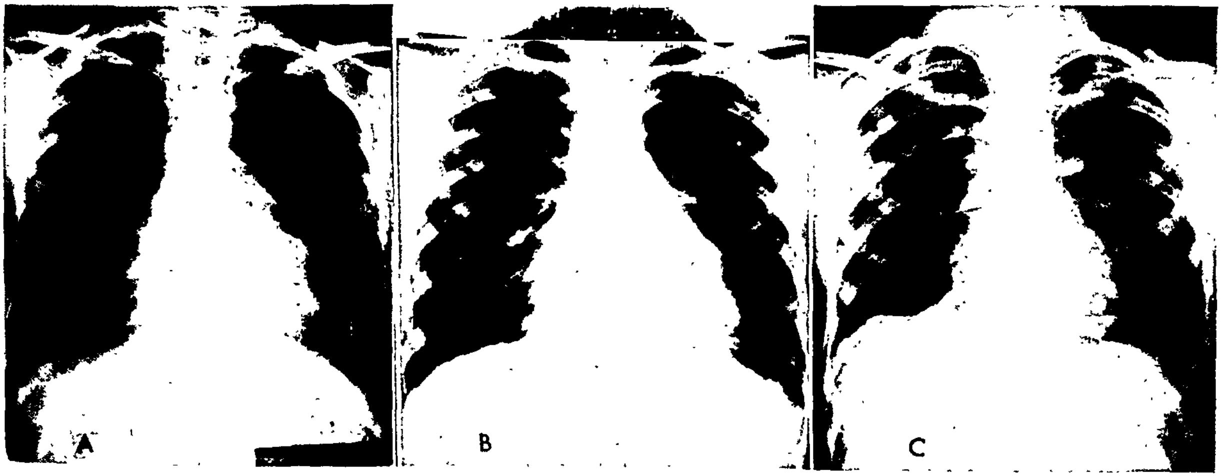

Fig. 2.—Posteroanterior teleroentgenograms in case of acute pericarditis. *A* (4/12/57), moderate enlargement of cardiac silhouette, with blunting of both costophrenic sulci; lung fields clear. *B* (4/25/57), sulci clear and cardiac silhouette smaller. *C* (5/1/57), cardiac silhouette and lung fields normal, with clear costophrenic sulci.

Summary

The problem of differentiating acute myocardial infarction from acute pericarditis is made more difficult when the latter presents an electrocardiographic picture of localized rather than generalized ventricular injury. We have called this the "pseudo-infarction" phenomenon and its three major characteristics are as follows: 1. The S-T segment elevation is confined to leads reflecting a relatively small ventricular area. 2. Reciprocal depression of the S-T segment occurs. 3. Major QRS changes may be seen. As illustrated in the case reported and a similar case cited from the literature, the electrocardiographic picture may resemble myocardial infarction so closely that the latter is distinguished with certainty only by the appearance of pathological Q waves.

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CLINICAL NOTES

ACUTE THROMBOCYTOPENIC PURPURA IN INFECTIOUS MONONUCLEOSIS

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The occurrence of cutaneous purpura in infectious mononucleosis has been observed for years but was first documented in 1923 by Downey and McKinlay.[1] Previously Longcope,[2] in 1922, called attention to the abnormal bleeding which often occurred in infectious mononucleosis. Actual thrombocytopenia in infectious mononucleosis was noted by Cottrell.[3] The low platelet count in his patient was not accompanied by hemorrhage. The first case of thrombocytopenic purpura complicating infectious mononucleosis was recorded in 1942 by Magner and Brooks.[4] Subsequently, at least 23 additional cases of infectious mononucleosis with thrombocytopenic purpura have been described.

Usually, other symptoms of infectious mononucleosis are present prior to the onset of the bleeding phenomena. These include sore throat, malaise, headache, cervical lymphadenopathy, and fever. Thrombocytopenic purpura is an uncommon complication of this disease, but because of the potential danger of cerebral and renal hemorrhage its early recognition is mandatory. This is especially true, considering the favorable response to treatment in two recently reported cases, one in a patient treated with adrenocorticotropin[5] and the other in one treated with cortisone.[6]

Report of a Case

A 25-year-old man was admitted to Vanderbilt University Hospital for the third time on May 14, 1958. His first admission had been in October, 1956, when he had complained of abdominal pain and at laparotomy was found to have mesenteric lymphadenitis. An appendectomy was performed. In February, 1957, a pilonidal sinus was excised. All hematological studies gave normal results on each of these admissions.

He had been in good health in the interim except for a chronic cough, attributed to cigarette smoking. In December, 1957, he had a small hemoptysis. Ten days before hospitalization a cough preparation containing codeine was prescribed. On the morning of admission his cough was productive of a few cubic centimeters of bright blood. This was followed by epistaxis. He then noted scattered purpuric areas over his trunk and all extremities, and there were also some petechial lesions. There was no previous history of any hemorrhagic tendency. He had had no sore throat, fever, malaise, or other systemic symptoms.

He did not appear acutely ill. His temperature was 97.4 F (36.1 C), blood pressure 140/80 mm. Hg, and pulse 96 and respirations 16 per minute. Numerous purpuric areas, 0.5 to 3 cm. in diameter, were noted over the trunk and the extremities. Several small anterior and posterior cervical lymph nodes were palpable but not unusually enlarged. There was no gingival bleeding. Scattered petechiae were present on the buccal mucosa. Numerous coarse, moist rales were heard throughout both lung areas. The heart was normal, and the liver and spleen were not palpable. The result of the neurological examination was normal.

Results of pertinent laboratory studies included white blood cell count 9,600 per cubic millimeter, with 5% juvenile and 57% segmented neutrophils, 1% eosinophils, 24% lymphocytes, 8% atypical lymphocytes, and 5% monocytes. Platelets were scarce

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on the smear. The hemoglobin level was 14.8 Gm.%, and packed-cell volume 43%. (Serial blood cell counts are recorded in the table.) The platelet count was 4,000 per cubic millimeter. The urine showed a specific gravity of 1.026; there was no albumin, but an occasional white blood cell was noted on microscopic study. Coagulation studies revealed a bleeding time of 17.5 minutes (Duke method) and a clotting time of 16 minutes (Lee-White). The L. E. cell phenomenon was not present as determined by the rotary method. The total serum bilirubin level was 0.4 mg.%. The cephalin flocculation test result was four + in 24 hours, the thymol turbidity 6.5 units, and the bromsulfalein retention 2% in 45 minutes. The alkaline phosphatase level was 4.6 Bodansky units. Result of the Venereal Disease Research Laboratory test on the blood was negative. Lumbar puncture disclosed clear spinal fluid, under normal pressure, with three white blood cells per cubic millimeter and a total protein content of 34 mg.%. Marrow aspirations showed no abnormality in the erythroid or myeloid series. An occasional atypical lymphocyte was seen, but these were not numerous. The marrow was thought to be essentially normal. The heterophil agglutination titer was 1:320 (unabsorbed). The heterophil antibodies in absorbed serum were positive in a dilution of 1:96.

Results of Serial Blood Cell Counts, per Cubic Millimeter

Date	White Blood Cells	Undifferentiated Myelocytes	Juvenile Neutrophils, %	Segmented Neutrophils, %	Eosinophils, %	Basophils, %	Lymphocytes, %	Atypical Lymphocytes, %	Monocytes, %	Platelets	Bleeding Time, Min.	Heterophil Agglutination*
May												
14†	9,600	..	5.0	57.5	0.5	0.5	24	7.5	5.0	4,000	17.5	...
16‡	13,100	1.0	9.5	55.5	..	1.0	29.5	..	..	19,000	14.5	1:320
17	...	..	..	..	..	..	..	..	..	58,000	6.5	...
18	...	..	..	..	..	..	..	..	..	...	8.5	...
19	14,500	..	1	67.5	..	0.5	16.5	7.0	7.5	94,000	..	1:320
21	...	0.5	0.5	64.0	0.5	..	16.0	11.0	7.5	195,000	..	...
22	...	..	..	..	..	..	..	..	..	...	9.5	...
23	14,200	0.5	2.5	72.5	..	..	6.0	14.0	4.5	201,000	..	...
26	13,200	..	2	73.5	1.0	0.5	12.5	4.0	6.5	163,000	..	1:320
28	10,300	1.0	7.5	59.0	2.5	1.5	16	1.5	11.0	128,000	6.0	...
June												
2	9,100	..	..	..	..	..	..	..	..	166,000	..	1:320
3	10,900	..	..	..	..	..	..	..	..	166,000	4.0	...

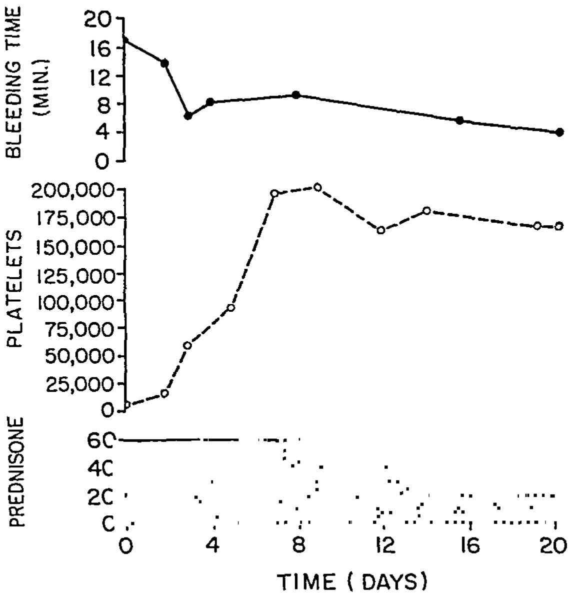
* terophil determinations done on 6/12/58 (1:96) and 7/1/58 (1:21).

†

‡ , 3.5%.

Because of the patient's persistent cough, bronchography and bronchoscopy were performed. The bronchograms were normal. The mucosa of the lower trachea and both main bronchi were fiery red and edematous. The findings were compatible with acute nonspecific bronchitis. Roentgenographic studies of the sinuses and chest were normal.

Treatment with prednisone was started on the day of admission. The patient received 60 mg. daily for eight days. There was an immediate and prompt rise in the platelet count (see figure), and the purpuric and petechial areas gradually disappeared. At no time was the spleen palpable. There was never any significant lymph node enlargement, and the patient was afebrile throughout his hospital stay. After eight days the dosage of prednisone was reduced to 40 mg. daily and 48 hours later to 20 mg. daily. Further reduction in dosage was effected, and the drug therapy was discontinued on the 36th day. The patient was discharged asymptomatic and has remained so to date.



Response of patient to treatment with prednisone (prednisone dosage given in milligrams; platelet count per cubic millimeter).

Comment

Thrombocytopenia and purpura, with epistaxis and hemoptysis, were the only symptoms in this patient. There was a complete lack of the usual physical findings associated with infectious mononucleosis. Yet the laboratory picture was diagnostic of the disease. Response to prednisone was prompt and is documented in the figure.

The cause of thrombocytopenia in infectious mononucleosis is not entirely understood. In our patient a careful study of the marrow did not show any abnormality of erythropoiesis or myelopoiesis. The megakaryocytes were normal. In other reported cases marrow examinations have not disclosed any cause for the thrombocytopenia. Dameshek and Grassi[7] attributed the thrombocytopenic purpura to a state of hypersplenism, with the spleen inhibiting formation of platelets from the megakaryocytes or preventing the release of platelets from the marrow. Another theory is that the spleen might destroy circulating platelets at an accelerated rate. However, in only one-half of the reported cases of thrombocytopenic purpura in infectious mononucleosis has there been demonstrable splenomegaly. Other studies on the etiology of thrombocytopenic purpura have pointed to the possible existence of a specific humoral factor in the plasma, such as a platelet agglutinin or lysin.[8]

Summary

The presenting complaint of a patient with infectious mononucleosis was thrombocytopenic purpura. The therapeutic response to prednisone was prompt and complete.

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ANTERIOR TIBIAL SYNDROME

A. Grunwald, M.D.
and
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The anterior tibial syndrome was first described by Vogt[1] in 1943. Further examples of this peculiar syndrome soon appeared. Horn[1A] published reports of two cases, Phalen[2] four cases, Hughes[3] three cases, Pearson[3A] one case, and Carter and co-workers[4] collected nine cases, two of which were fully documented. Blandy and Fuller[5] described three cases of necrosis of the leg muscles, naming the condition "March gangrene." In two of the cases only the peroneal muscles were involved. A review of the available literature showed that a total of 40 case reports have been published so far.

This condition usually appears in young males who are not used to exercising their leg muscles. After strenuous exercise, such as a game of football or a long march, in the case of soldiers, there is a sudden onset of severe pain in the anterolateral aspect of the leg, accompanied by swelling, to which redness is added after a few days. The patient is unable to move the foot or toes, and drop foot sometimes appears. There may be fever and leukocytosis, although generally these signs of inflammation are absent. Because of the severity of the pain the patient seeks medical advice early, and the doctor is led by the external signs to make a diagnosis of cellulitis, in the treatment of which incision may be performed. In the latter event a surprising finding is the absence of pus, while the underlying muscle is gray-brown in color, resembling boiled meat, and firm in consistency, as if fibrotic. As the number of cases so far described

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From the Surgical Department, Central Emek Hospital.

is not very large, and the condition is still not generally well known, we have considered it worthwhile to report a further typical example.

Report of a Case

A 16-year-old boy was seized with severe pain in the anterolateral aspect of the right leg while playing football, six days before admission. The pain forced him to rest for about a quarter of an hour. The pain then disappeared and he continued to play. The next day, while playing, he was again obliged to stop because of recurrence of the pain, which passed off after a short while. That night he was awakened by similar pain and found that he was unable to move his foot or toes. His doctor ordered hot compresses, which relieved the pain somewhat, but after two days' continuation of the pain he was given a local injection of procaine (Novocain) hydrochloride. After this treatment swelling and redness of the leg appeared with pyrexia (temperature of 99.1 F [37.3 C]). The doctor was unable to feel the dorsalis pedis and sent the patient to the hospital with a tentative diagnosis of acute suppurative myositis.

On admission there was redness and swelling on the anterolateral aspect of the right leg, with marked tenderness and hypesthesia on the dorsal aspect of the first four toes. The femoral, popliteal, posterior tibial, and dorsalis pedis arteries were palpable. He was able to move the foot and toes to only a limited extent. The temperature was normal, the blood sedimentation rate 34/60 mm. per hour (Westergren), and the blood picture was within normal limits. Result of oscillometric study of the leg was normal. On electromyography the anterior tibial and extensor hallucis longus muscles gave a reaction of degeneration. A diagnosis of anterior tibial syndrome was made, and it was decided to relieve the tension in the anterior tibial compartment by immediate operation.

With the patient under general anesthesia an incision was made on the lateral aspect of the middle third of the leg and on incision the fascia muscle, which appeared normal in color and consistency; was revealed. A second incision which was made parallel with and medial to the first revealed that the muscles of the anterior compartment appeared gray-brown, resembling boiled meat, and were of firm consistency. Muscle biopsy was carried out on both kinds of muscle exposed; the first was taken from the peroneal muscles, which appeared normal in color and consistency, while the second was obtained from the anterior tibial muscle, which appeared necrotic. Pathological examination of the biopsy specimens was reported as follows (fig. 1): The biopsy specimen of muscle consisted of two separate fragments measuring a few millimeters in size. Histological examination of the first specimen confirmed the presence of striped muscle bundles showing no special features. The second specimen showed patchy loss of striations, with some swelling and increase in the sarcolemmic nuclei in places. In one area a light infiltration of polymorphonuclear cells was present. The abnormal appearances in the second specimen were slight but sufficient to indicate early nonspecific degenerative change, the cause of which was not clear.

On the day after the operation the patient reported that the pain had practically disappeared, and the fever which appeared after the operation subsided in a few days. There was a discharge of necrotic material and muscle fragments from the operation site. Some of these fragments were subjected to pathological examination which was reported as follows (fig. 2): The material consisted of several irregular fragments of tissue, the largest of which measured 10 by 7 by 7 mm. Histological examination revealed the presence of striped muscle showing necrosis, with an acute inflammatory exudate extending from the necrotic area into the surrounding muscle bundles.

Fig. 1.—Photomicrograph of biopsy specimen, showing patchy loss of striations with some increase in sarcolemmic nuclei.

After a short time the pain disappeared completely, but movement of the foot and toes did not return, although there was no drop foot, and sensation in the toes returned and remained normal. The patient was discharged after 71 days and was seen weekly in the outpatient department. There was a progressive decrease in the discharge from the operative wound which eventually ceased completely, the wound healing by secondary intention three and one-half months after the operation. At the time of writing, six months after the operation, the movement of the toes and foot was still restricted, but the patient was able to walk with only a slight limp.

Comment

There are two main theories of the pathogenesis of the muscle changes. The first attempts to explain the findings on the basis of vascular changes, since the histological picture in the necrotic muscle is similar to that seen in Volkmann's ischemic contracture. Horn[1A] dissected the major part of the anterior tibial artery in patients with cases of the anterior tibial syndrome, and in some areas he found changes in the intima, media, and adventitia, with signs of obstruction. In most other instances, when the arteries have been examined histologically by other authors, similar changes have not been found. Also, in the majority of cases such evidences of impaired circulation as absent pulse or abnormal oscillometric or arteriographic findings have not been found. Vogt[1] has put forward the view that the necrosis of the muscle is attributable to vascular spasm. Mavor[6] opposed this view on the grounds that it is unlikely that vascular spasm will persist for a long enough period (6 to 24 hours) to produce actual necrosis. The occurrence in our patient of several attacks of pain on exertion which passed quickly on rest seems to support the theory of a spastic element.

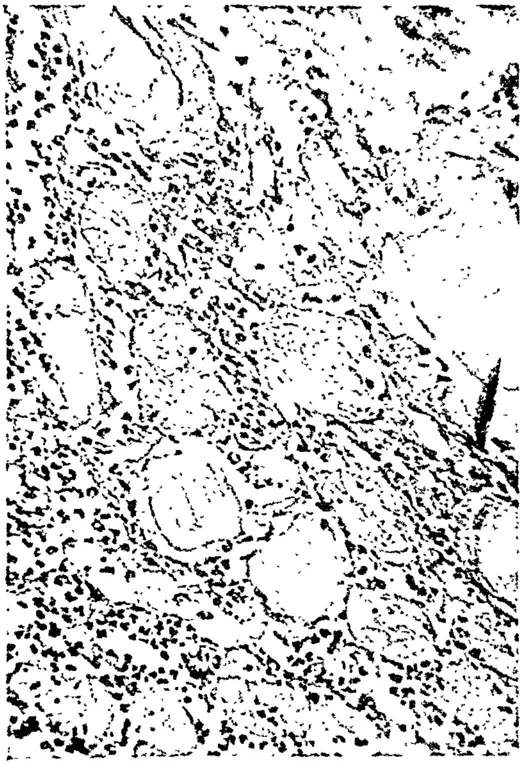

Fig. 2.—Photomicrograph of tissue sloughed from wound, showing necrosis with acutely inflammatory exudate.

The second theory, which is more generally accepted by investigators of the syndrome, is based on the anatomy of the anterior compartment of the leg. The special feature of this compartment is that it is practically closed, there being only a small opening at the level of the ankle. Within this enclosed space are the anterior tibial, extensor digitorum longus, and extensor hallucis longus muscles. If the tension in this compartment rises there is no possibility of enlargement to accommodate an increasing volume. It is known that overaction of muscle may result in an increase in volume of about 20%, because of fluid retention. Howard[7] believed that the retention is mainly of lactic acid. Small hemorrhages in the muscle also increase the volume. These factors produce a rise in tension in the compartment which impairs the circulation in the muscle and may lead to necrosis. Hughes[3] pointed out that this theory does not explain why only two or three muscles in the compartment are generally affected, namely the anterior tibial and extensor hallucis longus. Other authors have attempted to explain this discrepancy by the fact that the extensor digitorum longus receives a double blood supply from the anterior tibial artery and from the peroneal artery, whereas the extensor hallucis longus, which lies deep in the compartment, has a much poorer blood supply. It may be that all the factors mentioned play a part in the anterior tibial syndrome. Carter and co-workers[4] summarized the chain of events in the pathogenesis as follows: trauma of muscle → rise in tension in the compartment → changes in the blood supply to the muscles → ischemic necrosis.

The need for early diagnosis must be emphasized, since a reasonable cure may be achieved by keeping the leg at absolute rest if the changes in the muscle are not too advanced. A marked rise in tension in the compartment must be relieved by incising the fascia along the full length of the compartment. Even after such treatment the patients usually have difficulty in extending the foot and toes. Drop foot is not marked because of the contracture of the fibrosed muscles which tend to bring the foot into extension. Most authors use different orthopedic appliances in order to assist walking. Our patient is able to walk without difficulty and with only a slight limp. Mavor[6] suggested that a chronic form of the syndrome may exist which disappears without being diagnosed. He described the case of a professional football player who suffered severe pain in the anterolateral aspect of the leg for two years whenever the game was unusually strenuous. He found that a muscle hernia was also present. After operation the pain disappeared. Griffiths,[8] on the other hand, did not believe that the syndrome can take a chronic form. He pointed out that the pain in the anterolateral aspect of the leg is quite common at times of strenuous exertion and comments on the fact that in Mavor's case the pain disappeared after repair of the muscle hernia, which would produce the opposite effect of the usual fascial incision in cases of the acute syndrome. We are of the same opinion as Griffiths and would like to recall one of the patients described by Sirbu and co-workers[9] in whom signs of inflammation appeared five days after repair of a hernia of the anterior crural fascia, and the muscle was found to be necrotic and had to be excised.

Summary

The most probable train of events leading to the necrosis of the muscle in cases of the anterior tibial syndrome is as follows: unusual strenuous exercise of the leg muscles ➔ rise in tension in the compartment due to the increased bulk of the muscles resulting from edema, fluid retention, and small hemorrhages ➔ interference with the blood supply, leading to necrosis. In our case the possibility exists of vascular spasm's having played a role at the beginning of the illness. Early diagnosis and operation are important in order to insure the minimum of disturbance in walking.

The pathological examinations were performed by Dr. E. Levy.

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CORONARY OCCLUSION AFTER CARDIAC MASSAGE

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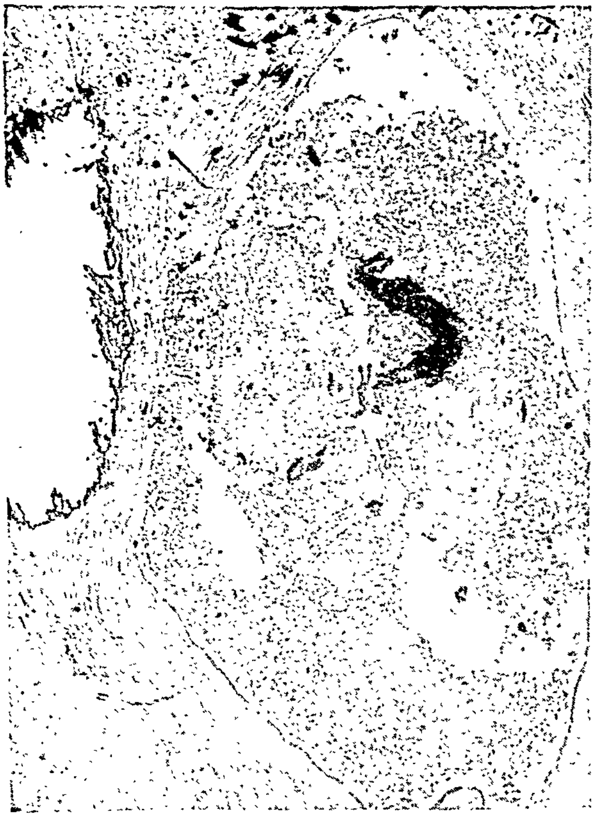
Manual massage of the heart for cardiac arrest is a dramatic event and is often lifesaving.[1] In view of the circumstances under which such massage is usually performed, however, it is not too surprising that structural changes in the heart occasionally result in the form of injuries to the epicardium, myocardium, endocardium, and small vessels.[2] The present report describes another kind of injury, which to the best of my knowledge has not been previously described, namely, the rupture of an atheromatous plaque of one of the coronary arteries, with subsequent occlusion and myocardial infarction.

Report of a Case

The patient was a 70-year-old woman who was subjected to surgical treatment for rectal bleeding on Nov. 25, 1958. A colostomy was successfully performed after resection of the rectal ampulla and distal portion of the sigmoid colon. Less than one hour after termination of the surgical procedure, respiration ceased and cardiac arrest occurred. Manual cardiac massage was started within a few minutes, and spontaneous heartbeat resumed 20 minutes later. However, the patient remained apneic, and artificial respiration had to be continued. She remained unconscious, breathing only with the help of a respirator. Pulse rate increased, and at the same time there was a progressive drop in blood pressure. She died on the second postoperative day, about 24 hours after operation.

The autopsy findings were recent myocardial infarct with occlusion of the descending branch of the left coronary artery, old myocardial infarction of the apex, bilateral pulmonary atelectasis due to mucus plugs, cerebral edema, cholelithiasis, and severe generalized arteriosclerosis. The most interesting histological finding consisted of an area of recent infarction of the left ventricular wall located distally to the occlusion of the descending branch of the left coronary artery. The myocardium showed a slight infiltration by scattered polymorphonuclear leukocytes, with blurring of striation of the muscle fibers. The coronary artery revealed a tear of the intima at the point adjacent to an atheromatous plaque which rendered a portion of the wall rigid while the rest of the lumen appeared somewhat flattened. There was formation of a clear space between the atheromatous plaque with its fibrous support, and the remainder of the intima showed the presence of red blood cells within the tear (see figure). The brownish pasty material obstructing the lumen of the artery at this point consisted of a mixture of red blood cells, cholesterol crystals, calcium, and fibrin. Since this kind of material was present in the plaque and could be traced through the tear of the vessel wall to the material occluding the artery, it is believed that the cardiac massage was responsible for the trauma to the atheromatous plaque which produced the occlusion of the artery. This was subsequently followed by the myocardial infarction.



Section of coronary artery with ruptured atheromatous plaque.

Summary

Manual massage of the heart was successful in restoring the heartbeat after cardiac arrest in a 70-year-old woman. As a result of the manual massage, the patient developed an acute myocardial infarction induced by rupture of an atheromatous plaque. Direct injury of one of the coronary vessels is a rare complication of cardiac massage.

375 Seguine Ave. (9).

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CAUSES OF DEATH IN PRISONERS OF WAR.—Among 209 prisoners-of-war who returned home severely malnourished, subsequently died, and were examined post mortem, the following causes of death were found (average percentage cause of death for the entire population in brackets):—Tuberculosis, 30.1% (3.5%); endocarditis, 12.5% (0.2–2.2%); liver disease, 9.1% (2.5%); renal disease, 6.7% (1.8%); and degenerative cardiovascular disease, 3.4% (19.0%). Although it was difficult to give a definite figure for the incidence of arteriosclerosis, it is felt that a clear-cut disposition would have been noted, but was not. Hypertension was a frequent finding during the convalescent stage after malnutrition, but it was a rare cause of death (7.1%; no comparative data available for population). Suicides were rare at 2.4% (4.7%); malignant tumours were found in 14.4% (21.5%); and gastro-intestinal disease in 3.8% (3.3%). The ages of these patients at the time of death had ranged from 25 to over 70 years.—A. Dietze, Late Sequelae and Causes of Death After Prolonged War Imprisonment and Malnutrition, *Deutsche Medizinische Wochenschrift*, July, 1959.

MEDICINE AT WORK

- *Flood, Fire, and Fury*
- Nine New York Doctors
- *PHS and the Basic Six*
- *Medicine of the Deep*
- *Medicine and the Atom*

Voice of Tomorrow

Before graduating from Sacred Heart High School in Elizabeth, N. J., last June, Miss Carol Pryor spent hours studying in the school library—but she found broader knowledge outside the window. She recorded that scene, and today is the 1959 winner of an essay contest sponsored by the American Association of Physicians and Surgeons. Miss Pryor's $1,000 award is for the best of several hundred local-winning entries of U. S. high school students on the topic, "The Advantages of the American Free Enterprise System." An excerpt follows:

"From the window of our school library I can see every day what I think is one of the greatest tributes to our American system of free enterprise—a well-used railroad transporting hundreds of freight cars daily, carrying state of Maine products, Florida fruits, oil, coal, livestock, scrap metal. Through the underpass a small truck farmer is bringing his produce to market behind a giant trailer truck. A huge oil truck pulls up alongside a gaily-painted florist's delivery car. Only by man's freedom to produce according to his capacity, and to consume or dispose of what he produces according to his own judgment, respecting the rights of others, has such progress been accomplished."

Judges in the contest were Dr. George C. Turner, president of the Chicago Medical Society; Arthur L. Conrad, president of the Heritage Foundation, and George C. Cooley, secretary of the A. M. A. Council on Medical Service.

Doctors of Defense

Washington Preview of A Plan for Survival

While the next war may be a push-button duel, fought impersonally with nuclear bombs and ballistic missiles, survival of the participants may well hinge on their ability to adapt to survival principles reminiscent of the stone age. It is this paradox that guides the Public Health Service's emergency health planning, a national defense function under delegation to it by executive order.

To determine PHS progress and to gain a look at the future, members of the A. M. A. Committee on Disaster Medical Care met in Washington last October for a two-day briefing. Dr. Carruth J. Wagner, chief of the division of health mobilization, told them that the PHS program can be classified in four categories: planning, training, testing, and operation; and to PHS, the most important of these is training. He said, "The first objective is the development of the capability of each individual to meet his own health needs. The second objective is to develop the capabilities of the community to meet its own health needs, using its own resources."

To accomplish this individual and communal self-sufficiency, according to Mr. Jerrold M. Michael, acting chief of the training branch, the division plans to promote the concept of "filtered-down" training. "This is a three-step program," he told his visitors. "Initially, the division staff itself will have to be brought up to the mark via inservice training in both the philosophy and technical

It may look like a medieval torture chamber, but it's actually an echo-free room used in sound research at the New London, Conn., Submarine Medical Laboratory. For a look at what's new in subsurface medicine see page 2219.

WORK

detail of program responsibility. Follow-through to the other two steps is based on an incentive plan in which commissioned reserves of the PHS and other selected health workers will form a paid cadre that can carry training down to the individual. This cadre will also provide a group of professional health workers who may be trained to accept additional health responsibilities in the event of a national disaster."

What kind of health responsibilities? PHS foresees:

–Nurses, dentists, veterinarians, pharmacists, and technicians being required to take over duties not normally theirs–arresting of hemorrhage, treatment of shock, reestablishment of patient airways, and other measures.

–Physicians and other key health workers having to assume the tasks of maintaining safe water supplies and overseeing waste disposal and sanitation.

–Science instructors, students, and food industry workers having to fill in for missing or overworked food and drug inspectors.

Whatever the substitute plans worked out for the maintenance of the health and well-being of Americans in time of disaster, they are all predicated on the assumption that the individual person is going to look out for himself during an initial period that may last from 18 hours to two weeks. Just what demands will be made on him during this first phase is now under study. Dr. Robert L. Smith, assistant chief of the division, told the assembled physicians, "A research project is being conducted at the Public Health Service hospital at Boston which will result in a determination of the health knowledge which is necessary in each individual for that person to meet his own health needs and the needs of others through self help, family help, or neighbor help in the post-attack period." Some of the knowledge, he said concerns first aid, but perhaps of more importance are basic survival techniques.

While PHS has been busy with the subject matter of such disaster teaching, the U. S. Office of Education has been concerned with putting into motion the machinery for instruction. Walker Agnew, Ph.D., chief of the section on civil defense education, said his office now has contracts with school officials in four states–Florida, Kentucky, Texas, and Minnesota–for the training of lay teachers who will in turn educate laymen through adult education courses.

Despite repeated and increasingly dire warnings of the dangers of unpreparedness in event of nuclear war, public apathy is still a major problem for the planners–but not a forgotten one. One of the division's many research projects, according to Dr. Nicholas C. Leone, chief of the research branch, is one entitled "Factors of Resistance in the Acceptance of and Participation in Civil Defense Activities."

Flood, Fire, and Fury Are Testing Medicine's Civil Defense Role

Well-planned civil defense at the community level gives medicine an effective weapon for coping with peacetime disasters which may strike anywhere, anytime. Some of the same suffering which the whole nation would undergo from a nuclear, biological, or chemical attack is experienced on a small scale from floods, fires, storms, and accidents.

This viewpoint was stressed repeatedly at the 10th County Medical Societies Civil Defense Conference in Chicago, Nov. 7 and 8. The meeting, sponsored by the A. M. A. Council on National Defense, drew 275 men and women from 33 states (including Hawaii), the District of Columbia, and Canada.

Dr. Paul A. Slattery of Orinda, Calif., described civil defense as "the civil population protecting itself and keeping to a minimum the consequences of a disaster from whatever source." Physicians, as the body of private citizens most directly involved, must take the lead, said Dr. Slattery.

Two other speakers reported a contrast in results of a test of disaster plans in the past year:

–Dr. James E. Segraves, director of the disaster plan at St. Anne's Hospital, which received 46 of the 100 victims hospitalized after a parochial school fire in Chicago last December, said all were bedded down and under definite care within four and one-half hours of the fire. The plan had been in the making for seven years and frequent drills had been held. He pointed out that teamwork and simplicity are vital to the success of any disaster plan, and said, "Duties of all participants, including nonprofessional help who lack medical knowledge, must be outlined in simple terms."

–Dr. Curtis H. Lohr, civil defense medical and

Split-Level Hospital

A New Jersey hospital, being built so that in the event of atomic attack it can function entirely underground (The Journal, Aug. 23, 1958, page 2082), has received a special federal grant of $400,000. Leo A. Hoegh, director of the Office of Civil and Defense Mobilization, said the grant, first of its kind, is to help St. Barnabas Hospital for including the fall-out shelter in the new building at Livingston, N. J.

Two of the six floors in the 10-million-dollar health center will be below ground level. The four upper stories will be composed mostly of convalescent wards. The two lower stories, to be sealed off in the event of an attack, will contain the operating nucleus of the hospital. The two lower levels will have five acres of floor space and be able to serve 1,000 bed patients and many more ambulant patients.

hospital chief for St. Louis, said 56 privately owned ambulances supposedly available for disaster service remained idle after a pre-dawn tornado last February. Nearly four hours elapsed before authority was received to activate civil defense field units. By then it was too late; all 21 dead and 247 injured had been moved in city ambulances and police cars. Dr. Lohr believes that a breakdown in communications, frequently cited as a weak spot in disaster work, may have increased the loss of life. A series of delays occurred in notifying the proper authorities of the tragedy in St. Louis, and as a result a five-month-old disaster plan remained unused.

While civil defense in both war and peace was discussed, Dr. Joseph R. Shaeffer of San Antonio, Texas, felt that preparedness for any catastrophe has a single base. He said, "It is not necessary to dwell constantly on the medical problems of atomic warfare. Major disasters . . . are daily experiences. Any community organized and prepared to meet a major disaster, including atomic disaster, with an all-inclusive plan, will find little difficulty in meeting its responsibilities in event of a disaster of lesser magnitude."

Dr. Harold C. Lueth of Evanston, Ill., is Chairman of the A. M. A. Committee on Disaster Medical Care of the Council on National Defense. Other members are Drs. Wayne P. Chesbro of Berkeley, Calif.; Cortez F. Enloe Jr. of New York City; Carroll P. Hungate of Kansas City, Kan., Francis C. Jackson of Pittsburgh; Mass L. Lichter of Melvindale, Mich.; David Henry Poer of Atlanta; and Charles W. Steele of Lewiston, Maine. Staff secretary is Mr. Frank W. Barton of Chicago.

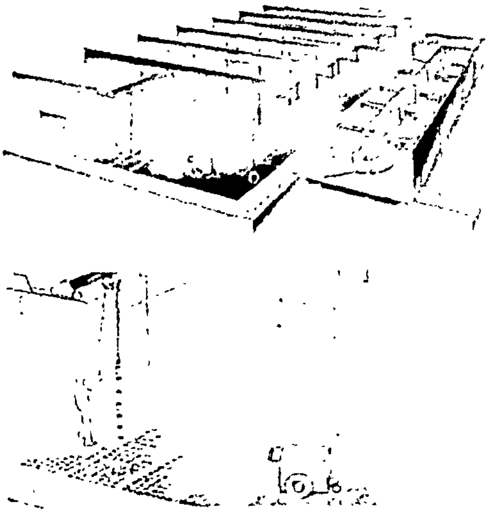
Biochemists, Physicists, Engineers, Physicians

Much Sweat but No Tears Are In This Teamwork on Blood

Teamwork involving an industrial firm, a government agency, a medical school, and scientists in medicine and related fields is being credited with a long-term blood storage project which may ultimately revolutionize all present concepts of blood banks.

Taking part in the advanced research program for storing whole blood at —320 F (—271 C) are physicians from the University of Buffalo Medical School, the Office of Naval Research, and biochemists, physicists, and engineers assembled by the Linde Company in its laboratories at Tonawanda, N. Y. Company officials announced late in October:

"At the present stage of development—with much additional work to be done—blood in volumes of 1 pt. can be frozen solid in fewer than 45 seconds. With approximately equal rapidity it can be thawed to body temperature for transfusing. Present data indicate that blood stored at this temperature [that of liquid nitrogen, the cooling agent] may be preserved indefinitely. This project is vitally important to civil defense, to the military, and to the public at large."



Artist's concept of the regional blood bank of the future, showing close-up detail of actual storage procedure. Individual blood containers are kept in honeycomb storage chambers in floor of building. These are refrigerated by liquid nitrogen which circulates beneath holding area. Rapid thawing equipment is in right-hand wing of the building.

Scientists at the company, which is a division of Union Carbide Corporation, say that the quick-freeze process has resulted in red blood cell survival rates of 75 to 85% after thawing but before transfusing. They are now examining the system for use in the preservation of such other tissues as marrow and bacterial cultures. Said Dr. R. M. Milton, manager of the company's research laboratories:

"Based on present knowledge we visualize a process in which freezing or thawing can be carried out by hospital technicians in considerably less than five minutes per unit of blood. It will be possible to design inexpensive, sterilizable, 1-pt. containers with suitable heat-transfer characteristics for freezing, storing, and thawing blood to provide a process suitable for general medical use."

Los Alamos Laboratory

Occupational Health Challenge With a Big Difference

Los Alamos Scientific Laboratory, perched high on a rocky mesa in northern New Mexico, is a place born to violence. Built in 1943 for the express purpose of creating an atomic bomb, it came of age as mushroom clouds obliterated the sun over Hiroshima and Nagasaki. Today its activities are more diversified but no less potent. Research into weapons, power reactors, nuclear propulsion, and explosives still provides the elements for potential disaster.

It is with no little pride, then, that Roy Reider, laboratory safety engineer, maintains that "the greatest safety hazard confronting Los Alamos workers is still the automobile." Reider was one of a dozen scientists and technicians who spent a day and a half last October briefing members of the A. M. A. Council on Industrial Health on the plans and operations of the laboratory's health division, headed by Dr. Thomas Shipman.

Norris Bradbury, Ph.D., director of the laboratory, which is operated by the University of California, laid the problem on the line for his visitors. He said, "We have every known industrial health problem here, with the possible exception of silicosis, and we're keeping an eye open for that." Whatever common hazards may exist in the laboratory's day-by-day operations, however, the specter of plutonium contamination is the prime Los Alamos concern. To make the staff presentation more easily understood, Dr. Shipman and his associates keyed their discussions to plutonium—its production, its widespread use at Los Alamos, its handling difficulties, and its hazardous nature.

Lab Bench to Building

"I recently received a lapel pin signifying 15 years of service at the lab," said Wright Langham, Ph.D., leader of the biomedical research group. "It is plated with gold, but it might more appropriately be wrought of plutonium. In 1943, I'd never heard of the stuff, but now I know that I shall never get away from it." Dr. Langham's first task at the laboratory was the refinement of methods of detecting exposure of personnel to plutonium, and he is still at it. He says, "We started out with one-half of a lab bench, and now we have a 2-million-dollar building." But lab bench or four-story building, the research group's major interest is still the biomedical detective story—establishing the permissible body burden of plutonium. Of greatest help with this task has been the follow-up of early laboratory employees who have had a wide range of exposure. Many of these have moved away, but a number of them have agreed to take part in the research effort by submitting to periodic examinations.

Laborious and painstaking work has resulted in a body of data that has been put to use effectively in the protection of Los Alamos workers. Dean Meyer, leader of the health physics group, says, "Our job is to take the laboratory findings and use them as a base for devising workable monitoring systems." The health physicists design equipment and determine methods of handling materials. One difficulty has been to collect air samples reasonably representative of the air breathed by the workers. To do this, the physicists have designed a sampler they call a "giraffe." A motorized pump mounted on wheels, it sports a long intake neck that pokes over the worker's shoulder and inhales a sample of the air he is breathing. This and other methods of sampling not only warn of intermittently high concentrations of plutonium particles but measure every worker's exposure. These exposure records are kept in the employee's cumulative health file, where they aid the physician in determining when the worker should be relieved or removed to an area involving less exposure. Other safeguards include the wearing of disposable clothing on the job and a variety of shielding devices.

Visiting physicians listen attentively as a staff member at the nuclear medical laboratory explains some of the health hazards faced at Los Alamos.

Combination of Risks

The work of the laboratory's health physicists complements that of the industrial hygienists. Dr. Shipman described the hygienist as "both chemist and engineer—a Janus looking in both directions at the same time." Much of the looking of the hygienists is done at the hundreds of air samples taken daily and at the vast array of equipment used to monitor the laboratory atmosphere and contain its deadly by-products.

Helping to prevent high concentrations of plutonium particles and doing something about those that do occur are the functions of the safety group. Plutonium, according to Mr. Reider, poses a unique combination of risks: It is inflammable, it is easily contaminated, and it is expensive. Its inflammability and its cost combine to make laboratory firefighting a difficult procedure. The use of firefighting compounds in certain work areas may so contaminate plutonium that has been expensively purified that small fires are often allowed to burn themselves out under supervision. To cut down on the possibility of wounds which might be contaminated by plutonium, Mr. Reider says the laboratory uses "kindergarten techniques." He told his audience: "Just as the small child is given blunt scissors to prevent puncture wounds, so we aim to make it as difficult as possible for workers to injure themselves with tools and instruments."

Laboratory accidents not only endanger people but in some cases contaminate valuable equipment. Such contamination necessitates one of two things at Los Alamos: decontamination or disposal, in that order. Decontamination techniques—practiced by a five-man crew in the health physics group—are of a wide variety, but all have a common ingredient—hard work. Soap and water scrubbing is one method. Sandblasting is another. Degreasing compounds are employed, as is ultrasound cleaning in some instances. On occasion, the crew has erected a plastic tent around an area of contamination to contain it and then donned plastic suits in which to go about their clean-up work.

Into the Rio Grande

One result of decontamination—and many other laboratory procedures—is a quantity of plutonium-burdened waste which must be disposed of. Solid matter is simply buried in a "hot" dump, but liquids present more of a problem. The laboratory has two sewerage systems: a sanitary sewer of the common, garden variety and a so-called acid system into which all lab sinks, tubs, and drains empty. Disposal of waste from the acid sewer is handled by a treatment plant similar to that used for ordinary sewage, except that all plutonium is precipitated into sludge, canned in 50-gallon drums, and buried in the dumping area. The liquid effluent empties into the Rio Grande, which is subjected to daily monitoring for pollution.

Despite their complexity, the purpose of all operations of the health division is the protection of people—a duty that Dr. Shipman and his staff take seriously. He and his fellow scientists not only direct the operations of the division but must apply its scientific findings for the protection of the people who work at laboratory jobs. Sound judgments on matters of health and safety must be rendered in an area where experience and precedent are either limited or totally lacking. This responsibility demands teamwork, and although staff members are split into groups for operating convenience, they form a closely knit team. So close are they, in fact, that a visitor once asked if overlapping functions did not produce frictions between groups. "I didn't quite know how to answer that," Dr. Shipman said, "so, as we toured the building, I put the question to many of the men. Summed up, their combined answer is 'I've got so much to do that anybody who wants a piece of my territory is welcome to it.'"

Dr. William P. Shepard of New York is Chairman of the A. M. A. Council on Industrial Health. Dr. Robert A. Kehoe of Cincinnati is vice-chairman. Other members are Drs. V. C. Baird of Houston; Rutherford T. Johnstone of Los Angeles; E. S. Jones of Hammond, Ind.; Lemuel C. McGee of Wilmington, Del.; Melvin N. Newquist of West Cornwall, Conn.; Oscar A. Sander of Milwaukee; Charles F. Shook of Toledo; James H. Sterner of Rochester, N. Y.; and Jan Tillisch of Rochester, Minn. Dr. B. Dixon Holland is staff secretary.

Submarine Medicine

Problems Multiply as Man Goes Deeper, Stays Longer

The submarine lay on the sea bottom off Key West in 322 ft. of crystal-clear water. Two men, dressed only in Mae West life jackets, entered its escape trunk, flooded down until they were neck-deep in water, and then valved in high-pressure air until the combined pressures equaled that of the sea outside. Opening the hatch, they rocketed to the surface—exhaling continuously—in 53 seconds.

It is significant that one of the two men to make the historic ascent—from more than twice the depth previously recorded—is a physician, Commander George F. Bond, chief of the U. S. Naval Medical Research Laboratory at New London, Conn. And it was Commander Bond who was host three days later on Oct. 6 and 7 to the A. M. A. Committee on Military Medical Affairs, when it met at the submarine base for a briefing on the medical problems that face man when he goes beneath the sea.

The areas of major medical interest became apparent as members of the Committee listened to reports on the operations of the several branches of the laboratory:

Audition—What happens to a man's hearing when he spends long hours on duty in the cacophonous thunder of a sub's diesel engine room? According to J. D. Harris, Ph.D., of the New London laboratory, he is a prime candidate for hearing loss, unless mechanical means are used to prevent it. One highly effective method is the use of a set of super ear muffs designed at the lab. Looking like halved oranges, the muffs have a soft rubber cuff, which acts as a seal, and are filled with foam plastic. The invention of such silencing aids is only a side line for Dr. Harris and his assistants, however. In a

Going to sea in a submarine's engine room is noisy as working in a boiler factory, a fact impressed on members of A. M. A. Committee on Military Medical Affairs as they take test dive on USS Crevalle.

suite filled with reverberation rooms and echo-free chambers, they seek the basic facts of sound perception so necessary in an age when submarines depend almost wholly on sound detection for survival (see photo).

Personnel Assessment—What makes a sailor volunteer (as they all do) for the rugged life aboard a submarine—higher pay, better food, improved status, or less obvious reasons? B. B. Weybrew, Ph.D., chief of the laboratory's personnel branch, spends much of his time devising and testing means for determining this and other psychological mysteries. He told the Committee, "When it costs thousands of dollars to train a submariner, you want to know as much as possible in advance about the probability of his staying in the service." To do this, Dr. Weybrew and his staff test the men with everything from straightforward questions ("Why did you join the submarine service?") to checks on preferences in humor ("Do you chuckle at a cartoon showing a woman wiring her hammock-snoozing husband to a lightning rod as thunderclouds gather overhead?").

Physiology—Is the 24-hour cycle a natural one for the human mind and body or is it too short—or too long? The question may seem academic to a man whose days are geared to the solar cycle, but to Dr. K. E. Schaefer, the question is a pertinent one—he is concerned with the scheduling of watches aboard a missile-firing submarine that may remain beneath the sea for three months or more. Not all of the laboratory's physiological interests are so nebulous, however. Such problems as air embolism in deep-water escapes, nitrogen narcosis in diving, and carbon-dioxide tolerance form the day-to-day work of the physiologists.

Vision—Does the use of red lighting beforehand help a man's night vision when he goes on deck? Recent experiments have convinced F. L. Dimmick, Ph.D., that it does, but not to the extent previously believed. Until recently, submariners thought that red light exposures of up to one-half hour prior to surfacing were an aid to night sight. Dr. Dimmick says laboratory studies now indicate that maximum values are reached after a 10-minute exposure and that eyes not previously conditioned adjust 3 minutes slower than those having the benefit of red lighting.

Nautical Newcomers

It wasn't all lecture and theory when the A. M. A. Committee on Military Medical Affairs went to New London in October. They and a staff writer for The Journal also got a good look at what life inside a submarine is like.

After a keel-to-conning-tower tour of the nearly completed nuclear submarine USS George Washington as it lay at its Thames River pier, the group then boarded the USS Crevalle for a four-hour run both above and below Long Island Sound. The Crevalle is a fleet-type World War II sub credited with the sinking of 22 Japanese ships. She is now used for training purposes.

Commander Bond, a former member of the A. M. A. Council on Rural Health, characterized the laboratory's research work as "80% basic and 20% operational," but he is a man who obviously enjoys some of the more physical aspects of applied research. In addition to the record submarine escape ascent, he has also made underwater tests of gear designed to help jet pilots free themselves from planes downed in the sea. A pet project he is currently plugging is a comprehensive exploration of the nation's coastal continental shelf by divers who would use a submerged and pressurized headquarters. Such a method would mean greater productive bottom time for divers, who thus would be freed of long hours of decompression that are necessitated by surfacing after each dive.

Influencing all current research on submarine problems is a concept that emerged when the first nuclear-powered sub slid off the ways at New London. Commander Bond states it this way: "A submarine used to be viewed as a surface vessel that could submerge. Now it must be looked on as an underwater vessel that can surface. There's a big difference."

Dr. Richard L. Meiling of Columbus, Ohio, is Chairman of the A. M. A. Committee on Military Medical Affairs. Other members are Drs. Reuben A. Benson of Bremerton, Wash.; Joseph B. Copeland of San Antonio, Texas; Henry A. Crawford of Cleveland; Gerald D. Dorman of New York City; Perrin H. Long of Brooklyn, N. Y.; Walter B. Martin of Norfolk, Va.; William B. Walsh of Washington, D. C.; and Herbert B. Wright of Cleveland.

Nine New York Doctors And A. M. A. Membership

There are more than 30,000 physicians in the state of New York. Most of them are members of the American Medical Association. Some are not. On Sept. 19 the A. M. A. Committee on Medical Facilities met in New York City with nine of the state's physicians to discuss why this is so—not only in New York but in the 49 other states as well. The nine were asked:

—Should the A. M. A. attempt to serve all doctors of medicine, or only those in private practice?

—If the A. M. A. is to represent all physicians, what needs to be done to make membership possible for and attractive to those who have not joined?

The two questions stem from one of the current major studies of the Committee, a subdivision of the Council on Medical Service: a study of the relationship of doctors who are in private practice to those who are not. Two years of Committee work have gone into the study, according to Dr.

Willard A. Wright, Chairman, who told his guests that the purpose of the New York visit was to try out a few possible recommendations on some of the Empire State's medical leaders.

The nine guest physicians—state and county medical society officials, medical educators, health officers, and medical directors—agreed that the A. M. A. should serve all physicians, regardless of type of practice. But most of them foresaw difficulties in such a course.

Dr. Norman Moore, president-elect of the Medical Society of the State of New York and dean of Cornell University Medical College, said, "Organized medicine must do away with intramural sniping if it is to retain the public's confidence, yet the gap between private practitioners and other physicians continues to widen."

Dr. Henry Fineberg, president of the state society and assistant commissioner of New York's public institutions, agreed. He said, "The programs of county and state societies are not geared for administrative groups. These men feel they are not wanted. This is a gap we must try to bridge."

One way to lure physicians in administrative positions into taking an interest in the A. M. A. is to make them feel needed, according to Dr. Gerald Dorman, medical director for an insurance company. He said, "We are on the right path if we can make these men feel their responsibility for bringing about a higher grade of medical care. We should stress the fact that they are all physicians and all have points of view on our problems."

One reason such men may not feel needed is simply because many of them know little about the A. M. A., said Dr. Waring Willis, a private practitioner from Bronxville. He noted that "Physicians not taking part in medical society activities know little about the A. M. A. except what they read in the newspapers." Dr. Willis suggested that discussions of A. M. A. activities might be incorporated into hospital staff meeting agendas to reach doctors who do not attend society meetings.

Dr. Herbert T. Wagner, executive director of the Medical Society of the State of New York, said lack of membership on the part of some physicians may stem from the simplest of reasons: lack of an invitation. He said, "As I look back, I can't remember the A. M. A. coming to me as a young doctor and saying, 'We want you in our organization.'"

Although their reasoning and opinions differed, all nine of the guest physicians agreed that the A. M. A. ought to urge county and state medical societies to remove membership limitations based on licensure and type of practice. If this proves impracticable, they said, then other ways of extending representational membership ought to be sought.

Members of the Committee on Medical Facilities listen as a medical educator discusses relationships between doctors in private practice and others.

That A. M. A. membership must be made appealing to those physicians who have not joined was emphasized by Dr. Wagner, who said, "There are those who say the additional dues make the difference. I say that an objection to dues is just a smoke screen covering more fundamental reasons for opposition to membership."

Chairman of the A. M. A. Committee on Medical Facilities is Dr. Willard A. Wright of Williston, N. D. Other members are Drs. William F. Costello of Dover, N. J.; Robert L. Novy of Detroit; David H. Poer of Atlanta, Ga.; John M. Rumsey of San Diego, Calif.; W. C. Stover of Boonville, Ind.; and Walter E. Vest of Huntington, W. Va. Dr. Edward C. Rosenow Jr. of Philadelphia is a consultant to the Committee. Staff secretary is Mr. George W. Cooley of Chicago.

Public Health and the Basic Six Concept

What is "public health?"

To the A. M. A. House of Delegates it is the six basic services enumerated in a 1950 resolution, but to Dr. John Porterfield, deputy surgeon general, it is "all facets of health which cannot be handled by individual endeavor." Dr. Porterfield is one of five physicians, all in the field of public health, who have accepted the invitation of the A. M. A. Committee on Medical Facilities to act as consultants in a current study. The five met with the Committee in New York in mid-September to aid in its survey of the current and future status of public health in the United States.

As to the Basic Six—vital statistics, public health education, environmental sanitation, public health laboratories, communicable disease control, and maternal and infant hygiene in cases in which private facilities are unavailable—the consultants agreed that they did not reflect public health as it is practiced today.

"Public health activities, as I would define them," said Dr. Thomas Hood, deputy director of the American Public Health Association, "are not limited to public health departments but are also carried on by voluntary agencies." Leadership in these various community health activities, he said, is a prime responsibility of public health officials.

Dr. Wilson Sowder, state health officer of Florida, agreed, but he noted that often the area of interest of a state department of public health is decided by legislative directive. He said, "We find that some of the things we want to do are opposed by legislation, and jobs that we would rather not have are imposed upon us."

Two of the consultants told the Committee that public and private health could not be so neatly separated as the House resolution would imply. Dr. Sowder said, "A public health officer could get into trouble just using the Basic Six. After all, preventive medicine is an important part of a pediatrician's practice."

Dr. Joseph Molner, health officer of Michigan's booming Wayne County, thinks many health problems demand attack from all sides. He said, "You can't turn a communicable disease program entirely over to the public health departments. Private physicians have to help by immunizing their patients."

One complaint about the Basic Six concept is that it makes no allowances for differences in population or geography. This was noted by Dr. L. L. Fatheree, vice-president of the American Association of Public Health Officials. He said, "Wherever people are, their medical needs must be met, although the organization and application of the practice of medicine is often beset by many difficulties."

In summing up his views on the role of public health agencies in the health care of the nation, Dr. Porterfield emphasized the difficulties of division. He said, "You cannot separate curative and preventive medicine. This study will be more enduring if it takes the future into consideration. The need is for fluid principles capable of absorbing unforeseen problems."

Friendly Debates Have a Common Goal—Better Health

Right or wrong, educators and physicians are "talking back" on such heretofore little-debated topics as periodic health examinations and physical fitness tests for the child in school. More than 200 of them from every region of the nation—representing medical societies, state health and education departments, and organizations interested in the health of school children—took part in and listened to debate which enlivened the Seventh National Conference on Physicians and Schools last month. Throughout, they were agreed on a common goal: better health and fitness for children. Some of their pros and cons were:

PRO—Periodic health examinations of children by physicians at schools are "very necessary," says Dr. I. P. Barrett of Fort Worth, Texas.

CON—"No," objects Dr. Ruth A. Lawrence, a Rochester, N. Y., physician. "They are unnecessary and outmoded and place too much emphasis on finding defects and not enough on correcting them."

PRO—National minimum standards of health knowledge, attitudes, and practice for school children can and should be set up so that health education in our schools can be evaluated. So says Dr. Charles C. Wilson of Yale University.

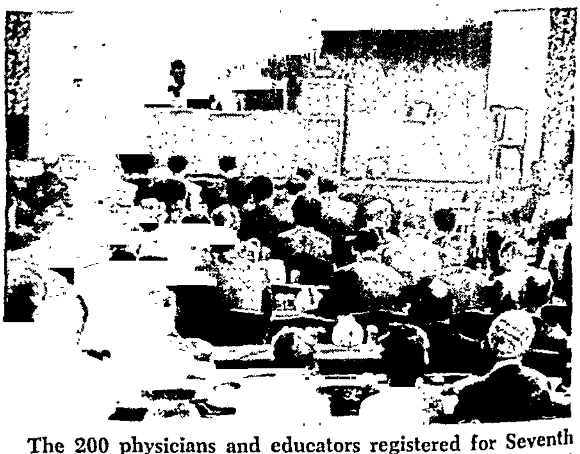
CON—But such standards would produce rigidity in the health education program and a loss of flexibility in curriculum planning, says Mabel Rugen, Ph.D., of the University of Michigan.

PRO—Physical fitness tests, insists Paul Hunsicker, Ph.D., also of the University of Michigan, can and should be developed on a national norm basis, just as intelligence tests are, and they would be valuable for both student and teacher.

CON—But such a national norm arrangement, protests Miss Elsa Schneider, a specialist for the U. S. Office of Education, might cause the statistics to become more important than the children.

In other presentations at the conference in Highland Park, Ill., on Oct. 13, 14, and 15, sponsored by the A. M. A. Department of Health Education, Dr. E. W. Pawsat of Fond du Lac, Wis., recommended that school children's excuses from physical education be signed by physicians rather than parents; Lloyd S. Michael, Ed.D., of Evanston, Ill., suggested that high schools pattern their curriculums more like colleges—with fewer formal classes and more individual study; and Dr. Harvey Flack, editor of *Family Doctor*, the British Medical Association's magazine for the public, urged that warnings about the probable relationship of cigarette smoking and lung cancer should be directed at school children rather than at adults.

Dr. Flack, himself a chain smoker of cigarettes, explained, "It is difficult to give up smoking; it is easier never to start."



The 200 physicians and educators registered for Seventh National Conference of Physicians and Schools, as they met at opening session.

Preventive Medicine Is a Medicolegal Matter, Too

One of the first American physicians sued for malpractice was Dr. John Pottes, accused in 1625 of causing a miscarriage by failing to satisfy his patient's craving for hogmeat. The fact that he not only was absolved of the charge but later was named governor of Virginia has led a present-day wag to crack:

"This shows that in those days judgments regarding doctors were collectibly low and collectively high."

In Washington, D. C., several weeks ago, a joint committee of the American Medical Association and the American Hospital Association met to discuss ways for physicians and hospitals to reduce grievances and claims, so that the healing arts may be practiced with minimum jeopardy to patients and maximum regard by the public at large. Here are some of the questions considered by the two-year-old A. M. A.–AHA Medicolegal Education Committee during its meeting Sept. 19:

–What can be done about "the growing problem of inadequate supervision of hospital residents?"

–Should minimum professional liability insurance for physicians be a requirement for hospital staff privileges?

–Are there ways to protect the "good Samaritan" physician from a damage suit when he is able to provide only first aid? (By coincidence, on the day that the A. M. A.–AHA group was meeting, a California law went into effect granting liability immunity for physicians rendering emergency care.)

–What can and should hospitals do to discipline staffs within the law?

–Which mechanism is best for impressing state medical and hospital associations with the importance of operating effective medicolegal education and review committees on a joint basis?

"These are pointed questions, certainly, and we do not yet have all the answers," says Dr. Joseph F. Sadusk of Oakland, Calif., the committee's first chairman (succeeded at the meeting by Dr. August H. Groeschel of New York City). "But we feel we are making headway with guide lines which view the patient from the specific standpoint of his safety—that is, to improve his care by preventing accidental injury or harm. We are reviewing and analyzing individual cases so that causative factors may be ascertained and preventive measures instituted. This is a matter of continuing education for physicians and others engaged in the care of hospital patients."

So far, such continuing education has taken the form of joint publication of appropriate articles in the official journals of both associations, preparation of a joint statement (still in process) on legal liability and insurance protection involving hospital medical staffs, and production of related motion pictures in cooperation with a Cincinnati pharmaceutical firm, the Wm. S. Merrell Co. The A. M. A.'s high regard for these educational efforts was indicated last June when the House of Delegates praised the committee and stated:

"It has become apparent that problems of professional liability cannot be dealt with apart from matters of patient safety, and a mechanism to minimize liability on the part of physicians and hospitals must be directed primarily to a reduction of incidents in the course of patient care which give rise to liability or potential liability."

Dr. August H. Groeschel of New York City is Chairman of the A. M. A.–AHA Medicolegal Education Committee. Other members are Attorney James E. Ludlam of Los Angeles and Mr. Ray E. Brown of Chicago, representing the AHA, and Drs. Henry I. Fineberg of New York City, H. Close Hesseltine of Chicago, and Joseph F. Sadusk of Oakland, Calif., representing the A. M. A. Staff secretary is Mr. C. Joseph Stetler of Chicago.

Members and guests discuss professional liability insurance at meeting of A. M. A.–AHA Medicolegal Education Committee in Washington, D. C.

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ASA GRAY, M.D.—COLLABORATOR OF CHARLES DARWIN

IN THIS centennial year of Charles Darwin it is interesting to note that Asa Gray, Doctor of Medicine, contributed heavily to the development of the theory of evolution that culminated in the fundamental concepts presented in "The Origin of Species" (Dupree, A. H.: Asa Gray, Cambridge, Mass., Harvard University Press, 1957). The first edition of this monumental volume was published in November, 1859. The presentation by Darwin was based on the painful accumulation of scientific information that had extended over several decades.

Asa Gray, Darwin's collaborator, was born early in the last century in the central part of New York State. Obviously he was a brilliant student, attested by the evidence that he began his formal education at the age of 3 years. He was exposed to Greek and Latin before he was an adolescent. After one year in a private academy in the Adirondacks, he abandoned undergraduate education and sought admission to the College of Physicians and Surgeons of the western districts in Fairfield, N. Y. Subsequently, he qualified for the degree of Doctor of Medicine. But he did not practice for long. In a manner similar to the intent shown by selected physicians of the ancient world, he developed an overwhelming curiosity in botany. This interest culminated in his appointment at the age of 32 years to the post of professor of natural history and director of the botanical gardens at Harvard College.

The quest for botanical specimens carried Gray about the world and provided a collection of flora that proved indispensable to the evolutionist in the interpretation of natural change. The initiative was taken by Darwin, and he inquired especially into the distribution of alpine plants in the United States as described by Gray in his "Manual of the Botany of the Northern United States." The correspondence resulted in the reliance by Darwin on the physician turned botanist for critical scientific data. The information on plants, transmitted by Gray, supported the theory of evolution generally and was used as basic source material in "The Origin of Species."

PHYSICIANS, HOSPITALS, AND NEW AND NONOFFICIAL DRUGS

Inquiries reaching A. M. A. headquarters reveal considerable confusion concerning the purpose of statements published under the title New and Nonofficial Drugs by the A. M. A. Council on Drugs. Indeed, the Council's statements, which appear regularly in The Journal and which are available in cumulative annual book form from the J. B. Lippincott Company of Philadelphia, are being interpreted by some persons and organizations as a form of acceptance, approval, or endorsement which is not intended. This erroneous concept apparently also has been used in some instances as a basis for authorization of purchases of hospital medication or allowance of hospital insurance payments for drugs. Undoubtedly a good deal of the misunderstanding stems from the former seal-acceptance program, under which the Council limited its descriptions of drugs to those considered to have well-established clinical usefulness. Accordingly, it is important to point out that the Council's current program for evaluation of drugs is designed to provide information concerning the status of all commercially available individual preparations of new drugs, whether or not clinical usefulness has been conclusively established.

The Council's revised method of operation was instituted in The Journal in 1955 and in the 1956 edition of its annual publication under the original name of the Council (Council on Pharmacy and Chemistry) and the former title, New and Nonofficial Remedies (New Program of Operation for Evaluation of Drugs, *J. A. M. A.* 158:1170-1171 [July 30] 1955). This circumstance also may account for some of the confusion between the Council's former and current programs. The subsequently instituted change in the name of the Council and revision of the title of its publication, which were made in The Journal early in 1957 and in the 1958 edition of the book, were designed to further emphasize its new method of drug evaluation and its primary concern with the clinical status of drugs. (Name of Council and Title of Its Annual Publication Changed, *J. A. M. A.* 163:645 [Feb. 23] 1957). Early this year, the introduction to Council statements on New and Nonofficial Drugs appearing in THE JOURNAL was reworded to explicitly disclaim their interpretation as an implied endorsement (Notice of Changes in Operation, *J. A. M. A.* 169:946-947 [Feb. 28] 1959).

It is appropriate to emphasize not only that New and Nonofficial Drugs is not a book of "accepted" or "approved" drugs but also that known trademark names of available brands are included merely as a matter of information to aid in the identification of drugs. The Council does not conduct clinical tests or laboratory analyses of drug preparations, or endeavor to compare the quality of various brands. Rather, the Council undertakes to comment on the proposed actions, indications, limitations, hazards, route of administration, and dosage of drugs, on the basis of existing available scientific data and reports of investigations. The compilation of authoritative information of this kind is designed to aid busy physicians who do not have the time to undertake their own appraisal of drugs. It also should be helpful to medical staffs in selecting drugs for hospital formularies.

One of the fundamental defects of the former seal-acceptance procedure lay in its encouragement of the faulty concept that accepted drugs were all "good" and unaccepted drugs, all "bad." The false sense of security engendered by this concept of acceptance actually fostered a careless attitude in the use of highly potent and effective agents having a narrow margin of safety between therapeutic and toxic levels of dosage. Thus, it became imperative that the Council's program be revised to place primary emphasis on the dissemination of early information, rather than the description of well-established drugs. Use of drugs on the basis of a symbol, such as a seal of acceptance, rather than on the basis of knowledge, should have no place in modern scientific medicine. The Council's current drug evaluation program, together with special reviews of therapy in various clinical disorders, and special reports and symposiums on special therapeutic problems, is aimed toward the encouragement of rational therapeutics as a part of the over-all effort to stimulate the continuing education of physicians.

THE GENERAL PRACTITIONER'S AWARD

Dr. Chesley M. Martin, a family doctor for the past 44 years in Elgin, Okla., was named general practitioner of the year by the House of Delegates of the American Medical Association at the Annual Clinical Meeting in Dallas on December 1. The Chairman of the Board of Trustees, Dr. Leonard Larson, presented a gold medal and a citation to Dr. Martin. The award is given each year to the physician who typifies the thousands of general practitioners throughout the country who have dedicated their lives to the practice of medicine and who have given exceptional service to their communities. Dr. Martin, who is 70 years of age, becomes the first Oklahoman to be so honored.

Chesley M. Martin, M.D.

Dr. Martin was born on a plantation in South Carolina on June 11, 1889. After completing premedical studies at Wake Forest, N. C., he attended Tulane University Medical School for two years. His final two years were spent at the University of Oklahoma School of Medicine, where he graduated in 1915. After practicing a short time in North Carolina, he returned to Oklahome and settled in Elgin. Dr. Martin began his civic activities the day he set foot in Elgin, and he has led the townspeople through a sustained period of development that has placed Elgin on a par with communities having several times its population and economic potential. He served 31 years as a member of the town board and is beginning his 42nd year as chairman of the school board.

As a result of Dr. Martin's interest in the activities of the young men of Elgin, the community has established an outstanding chapter of the Future Farmers of America. Dr. Martin's two sons are dentists; one daughter is married to a physician and another to an architect.

Dr. Martin's attitude is one of humble pride in his ability to help others. He has presided at the birth of 2,500 residents of the area, less than 500 of whom were born in the hospital. The regard in which he is held was summed up by a friend who said, "How lucky can the people of Elgin be? Dr. Martin has provided this entire area with faithful medical attention, all hours of the day and night, for as long as I can remember. He is a friend as well as a doctor."

ORGANIZATION SECTION

COPIES OF GUIDES TO EVALUATION OF PERMANENT IMPAIRMENT

The American Medical Association Committee on Medical Rating of Physical Impairment has announced the availability of copies of two guides dealing with the evaluation of permanent impairment. Copies of guides entitled the "Visual System" and the "Extremities and Back" can be obtained without charge by addressing a request to the committee at 535 N. Dearborn St., Chicago 10. The guides were published initially as special editions of The Journal of the American Medical Association during 1958. Those who desire copies of either or both of these guides are urged to have their requests in prior to Dec. 30, 1959.

The ad hoc committee of the Board of Trustees on Medical Rating of Physical Impairment believes that the following article will be of interest to all physicians.

Raymond M. McKeown, M.D., Chairman.

HOW SOCIAL SECURITY MEDICAL REPORTS ARE USED

William Roemmich, M.D., Baltimore, Md.

Since January, 1955, when the first disability provision in the social security law became effective, the Social Security Administration has received about one and one-half million disability claims. Four hundred and fifty thousand claims were received during the past year.

In practically all cases, the worker's attending physician furnishes a medical report. This report, together with reports from other physicians, hospitals, or clinics, provides the primary basis for determining whether the worker meets the social security requirements of disability.

The social security law defines disability as "inability to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or to be of long-continued and indefinite duration." In order to meet this definition and other requirements of the law the following conditions must be met.

1. The claimant's condition must be medically determinable—that is, it must be a condition that can be confirmed by medical examinations and tests.

2. The condition must be so severe that it prevents the person not only from carrying on his last or usual occupation but also from performing any substantial gainful activity.

3. The condition must have persisted for at least six months, despite therapy, and must be expected to continue indefinitely or to result in death.

4. The condition must not be remediable through treatment that is safe and reasonable according to usually accepted standards of medical practice.

5. The claimant must have a record of work under social security. In this connection, his work record must include a definite number of calendar quarters of social security coverage. This requirement is designed to limit disability benefits to regular workers who have been forced to stop work because of disability.

Medical Report Form for Doctor's Convenience

Disabled people apply for benefits at their nearest social security district office. That office gives a person information about his rights, helps him to fill out his application, and advises him about the proofs and documents that he may need to support his application. The disabled claimant has the responsibility to furnish, at his own expense, sufficient medical evidence for a reviewing physician to establish the presence of an injury or disease. This medical evidence should be in sufficient detail for the evaluation of the severity, duration, and remediability of the condition. The social security office gives the claimant an explanatory letter and one or more copies of a medical report form which he is instructed to take or mail to his attending physician

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Chief Medical Officer, Division of Disability Operations, Bureau of Old-Age and Survivors Insurance, Social Security Administration.

or any other physician, clinic, hospital, institution, or agency in which he has been treated for his condition. These reports are returned directly to the requesting office in the accompanying preaddressed envelopes.

The medical report form is furnished for the convenience of the physician, clinic, or hospital—doctors or institutions should not feel bound by its format or brevity. What is needed is a full clinical picture of the patient's condition. This requires a history and physical and supporting laboratory findings in sufficient detail to permit a reviewing physician to make an independent diagnosis and evaluate therapeutic possibilities as well as the patient's capacity for work. The information should be as complete as that which is usually obtained from the first clinic studies done for diagnostic and therapeutic purposes. If possible, a careful description of any limitations on the patient's ability to walk, sit, stand, bend, think, hear, see, and manipulate should be included. If the physician wishes, he may furnish the requested information in a narrative statement, using his own stationery instead of the form.

A well-prepared medical report can speed the determination of eligibility for disability benefits to a disabled patient. It will also avoid the need for more correspondence for additional clinical or laboratory data.

Determinations of Disability Made by States

The determination as to whether a claimant meets the definition of disability contained in the social security law is made, under federal-state agreement, by an agency of the state in which the claimant resides. In most states, this is the vocational rehabilitation agency.

The evaluation of disability is made in the state agency by a review team. One member of the team is a doctor of medicine, the other is a nonmedical member trained in disability evaluation. The determination of disability is a joint decision. The reviewing physician is primarily responsible for evaluating the severity, duration, and remediability of the "medically determinable impairment." The nonmedical member of the team evaluates the applicant's ability to perform substantial gainful work in the light of his education, training, work history, and demonstrated vocational skills.

The state evaluating team must decide whether the applicant is unable to engage in any substantial gainful activity due to a medically determinable condition which is expected to continue without significant improvement for a long and indefinite time. In carrying out this function, it is often essential for the state agency to arrange for, and purchase at government expense, independent medical examinations and tests to supplement information already on file from the claimant's own medical sources. This can be done only after the applicant has presented enough evidence that the reviewing physician believes it reasonably likely that a severe impairment exists. Consultative examinations cannot be used to relieve the applicant of his responsibility to submit medical evidence.

Consultative examinations may be purchased for one or more of the following reasons:

1. To obtain highly technical evidence believed to be necessary for sound evaluation by the reviewing physician and which the attending physician is unable to provide. Such evidence might be an actual measure of the applicant's capacity to consume oxygen at a specified rate.
2. There are medical reports in the file from two or more sources and the review team physician is unable to reconcile the separate pieces of evidence.
3. The attending physician's report describes severity (functional), remediability, or duration characteristics which in the opinion of the reviewing physician are inconsistent with the supporting history and physical and laboratory findings.
4. The attending physician's diagnostic, therapeutic, and prognostic conclusion, in the opinion of the reviewing physician, is not supported by history and physical and laboratory data, and attempts to obtain such additional information from the attending physician have not been successful.
5. The applicant gives notice of contesting his case at higher judicatory levels and the reviewing physician believes the case would be better supported or the attending physician's evidence strengthened with a second independent examination.
6. When the person is currently on the disability rolls and it appears that his disability may have ceased.

The state agency medical consultant or reviewing physician decides when a consultative examination is necessary, who is to make it, and the type and scope of the examination. When a physician is asked to perform a consultative examination he is advised that the government will pay his fee. State practice governs the amount of the fee. The examination may range from a simple laboratory test to a complete medical examination including work evaluation and complete diagnostic services.

State determinations are reviewed by the Bureau of Old-Age and Survivors Insurance for consistency and conformity to national policies. The bureau, however, is not empowered to reverse a state decision which is unfavorable to the applicant. Such a decision can only be reversed through the appeals process.

Claimant's Right to Appeal

Any claimant who does not believe that the decision on his claim is correct may ask that his case be reconsidered. In this event his case (including any additional evidence that may not have been presented earlier) will be carefully re-examined by both the state agency and the bureau. If the results of this reconsideration leave the claimant still dissatisfied, he may request a hearing before a hearing examiner of the Social Security Administration.

Of the one and one-half million disabled workers who have filed claims since January, 1955, only about 40,000, or less than 3%, have requested hearings before a hearing examiner. The hearing examiner makes a complete and independent review of the case, much the same as a judge in a court of law. At the hearing, the claimant may present the case himself or he may have a representative to help him. He and his representative have the right to examine all evidence made part of the record, including medical reports.

Where hearing examiners conducting hearings have found that additional medical information was necessary, attending or consulting physicians are asked to provide the required information in writing, rather than orally or in person. The hearing examiners request such information through the state agency. The state agency's request may go to the attending physician or a consulting physician. All requests for additional evidence are made to the attending physician. There are some exceptions which were discussed previously. In addition, qualified medical sources are available to the hearing examiner for securing advice and counsel.

A claimant who is dissatisfied with the hearing examiner's decision may take his case to the federal court. In cases before the federal court, no new testimony is taken from doctors or from others. The court merely reviews the record and decides whether the decision is supported by substantial evidence.

Doctor's Responsibility

Although his opinion is highly regarded and carefully considered, the attending examining doctor does not have to determine that his patient suffers a "disability." The law places this responsibility on the state and federal administrative agencies.

Misunderstandings occasionally arise because doctors sometimes append to their report conclusions such as: "My patient is permanently and totally disabled." As the foregoing discussion shows, the concept of disability includes requirements other than a disease and its characteristics. Therefore, conclusions based solely on clinical facts are sometimes inconsistent with those that have taken into account requirements in addition to clinical data. The doctor's report of the patient's chief complaint or of a physical finding can seldom be debated. A laboratory finding speaks for itself. Likewise, the doctor's observations that the patient can walk, stand, sit, bend, see, and the degree of efficiency with which he can perform these functions, are legitimate and important reasons for medical concern. This type of evidence provides the reviewing physician with a sound basis for determining whether the applicant has an impairment which, in the language of the law, makes him unable "to engage in substantial gainful activity."

By limiting himself to these kinds of clinical facts and observations, the examining physician avoids the need of committing himself with regard to either the "totality" or the "permanence" of his patient's condition. It is advisable for the physician to inform his patient that his report is limited to clinical facts and observations. The patient, then, cannot attribute an unfavorable decision to his doctor's report. Hence, any dissatisfaction which the applicant may have with the final determination will not be directed toward the doctor.

Vocational Rehabilitation.—All disability claimants are considered for possible services by the state vocational rehabilitation agency. The goal is to restore as many disabled persons as possible to the labor force. The doctor may want to keep this in mind when completing the medical report since he may have knowledge which would assist the rehabilitation counselor in planning and providing services for the patient.

Confidentiality of Medical Reports.—Medical reports furnished by attending doctors in connection with their patients' claims for disability benefits are of paramount importance in the successful administration of the social security disability program. As an integral part of the claim file, each report is safeguarded by the same legal restrictions which govern the confidential nature of all social security records. Only in certain authorized circumstances can medical reports be divulged. For example, medical information provided by the doctor may be made available to another government agency for use in developing a plan for the worker's rehabilitation. However, at a hearing before a hearing examiner, when the claimant is contesting the decision, the disabled person or his representative has the right to examine all the evidence on which the decision was based, including medical reports.

MEDICAL NEWS

ALABAMA

Dr. Sensenig Named Anatomy Chairman.—E. Carl Sensenig, Ph.D., was appointed chairman of the department of anatomy, University of Alabama Medical Center, Birmingham, during October. He succeeded James O. Foley, Ph.D., resigned. Dr. Foley continues as professor of anatomy.

ARIZONA

Psychiatric Seminar in Phoenix.—The Arizona Academy of General Practitioners in association with the Arizona Psychiatric Association has planned a psychiatric seminar for Feb. 13-14, in Phoenix. The principal speakers and their topics are as follows:

Dr. Frank F. Tallman, Los Angeles, "The G. P. and the Psychotic Patient."
Dr. Arnold R. Friesen, Los Angeles, "When to Treat and What to Refer."
Dr. Edward J. Stainbrook, Los Angeles, "Dealing with the Emotionally Disturbed Patient."
Dr. Allen J. Enelow, Los Angeles, (unannounced).

Information may be obtained by writing Dr. James L. Grobe, Chairman of the Mental Health and Liaison Committee, 5630 N. 27th Ave., Phoenix, Ariz.

CALIFORNIA

Internists Hold Annual Symposium.—The seventh annual clinical symposium of the Society of Graduate Internists of the Los Angeles County Hospital was held at the Statler Hilton Hotel and the Los Angeles County Hospital Oct. 30-Nov. 1. Guest speakers were Drs. Lauren V. Ackerman, St. Louis; Thomas Francis Jr., Ann Arbor, Mich.; Joseph B. Kirsner, Chicago; and David A. Rytand, San Francisco.

Hospital Addition Honors Pediatrician.—A pediatric addition to Mercy Hospital, Bakersfield, will be dedicated to the memory of Dr. Chester I. Mead, reportedly the first pediatrician of Kern County. Dr. Mead was past-president of the Rotary International and representative from California to Paris in the International Rotary Club's meeting of 1954. The hospital's pediatric addition is a spontaneous endeavor of a group of lay people, with advice from a Medical Advisory Committee. A modern, 24-bed department, it will be constructed above the fourth main floor at Mercy Hospital.

KANSAS

Dr. Hudson Appointed Assistant Dean.—Dr. Robert P. Hudson was appointed assistant dean, in charge of student affairs, of the University of Kansas School of Medicine, Kansas City. Dr. Hudson became an instructor in medicine in 1958 and was promoted to associate in medicine in July, 1959. His new appointment was effective Dec. 1.

MARYLAND

Dr. Brody Named Department Chairman.—Dr. Eugene B. Brody was appointed chairman of the department of psychiatry and director of the Psychiatric Institute of the University of Maryland School of Medicine, Baltimore. Dr. Brody joined the University of Maryland faculty in 1957 as professor of psychiatry and was appointed psychiatrist-in-chief to University Hospital and the Psychiatric Institute in 1958. Since the death of Dr. Jacob E. Finesinger in June he has been acting chairman of the department and acting director of the Psychiatric Institute.

MASSACHUSETTS

Radiologist Receives Gold Medal.—Dr. Frederick W. O'Brien, Boston, received the Gold Medal of the Radiological Society of North America from Dr. Laurence L. Robbins, also from Boston, retiring president of the society, Nov. 19 during the society's 45th annual meeting in Chicago. The medal is the organization's highest honor. Dr. O'Brien is a graduate of Boston College and received his medical degree from Tufts University in 1911. He is past-president of the Radiological Society and an emeritus professor of radiology in the Medical School of Tufts University.

Traineeships in Child Psychiatry.—The Walter E. Fernald State School was granted two traineeships in child psychiatry under the Training and Standards Branch, National Institute of Mental Health, Bethesda, Md., for physicians who want to complete their psychiatric education. The American Board of Psychiatry and Neurology approved one year of credits in neuropsychiatry for the board examinations. According to personal interests, the trainee has an opportunity to work in neuropathy, pediatric neurology, child psychiatry, or to engage in biochemical studies along with a general train-

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ing program. The training includes attendance of staff meetings at Boston hospitals. For details, apply to Dr. Clemens E. Benda, Director of Psychiatry and Research, Walter E. Fernald State School, Box C, Waverley 78, Mass.

MINNESOTA

Foreign Speaker.—Prof. C. F. W. Illingworth, department of surgery, Western Infirmary, Glasgow, [illegible] gave a lecture, "Choice of Treatment and [illegible] stic Implications in the Endocrine Approach [illegible] ast Cancer," at the Mayo Clinic, Rochester, [illegible] 19.

MISSOURI

Ceremonies Honor Dr. Strauss.—Dr. Paul Dudley White, Boston, spoke at ceremonies honoring the 70th birthday of Dr. Arthur E. Strauss, a member of the Jewish Hospital medical staff, St. Louis. Dr. White presented "The New Five Ages of Man" and conducted cardiology rounds. Dr. White lectured under auspices of the Arthur E. Strauss Visiting Physician Fund, which has been established in Dr. Strauss' honor through contributions of his patients. Dr. Strauss was honored at a dinner with members of the Jewish Hospital medical staff and Dr. White present. Dr. Strauss, a graduate of Harvard Medical School, has been a member of the Jewish Hospital medical staff since October, 1919. He is now consultant in medicine and cardiology at the hospital. He is also assistant professor of clinical medicine emeritus at Washington University School of Medicine.

MONTANA

Dr. Karnofsky to Give Lecture.—Dr. John A. Newman, secretary of the Mary E. Swift Tumor Clinic, Butte, reported that the fourth lecture will be held on March 26 at St. James Hospital, and the Finlen Hotel, Butte. Dr. David A. Karnofsky, Memorial Hospital, New York City, will be the guest lecturer and will discuss the "Chemotherapy of Cancer." All Montana physicians are invited.

NEW JERSEY

Photography Unit for Physicians.—Twenty-two doctors on the medical staff of Mountainside Hospital, Montclair, have organized a Medical Photography Club. The group meets the second Monday of every month. Inquiries may be addressed to the Medical Photography Club at Mountainside Hospital. Purpose of the club is to develop medical aide materials which can be used in a public information program in the area on medical care and medicine. Membership will be restricted to physicians living in the area served by the three Montclair hospitals, Mountainside, Community, and St. Vincent's. Associate memberships will be available to nonprofessional personnel affiliated with the hospitals.

NEW YORK

Health Commissioner Given Public Health Award.—Dr. Herman E. Hilleboe, Albany, state health commissioner, was awarded the Arthur C. McCormack award "for preeminence in the field of public health" at the annual meeting of the Association of State and Territorial Health Officers in Washington, D. C., recently. The last McCormack award was given in 1954. The award was established by the association to memorialize Dr. McCormack who was health officer of Kentucky and a public health leader during his lifetime. Recipients of the award must have had at least 25 years of meritorious service in the field of public health, of which 10 years must be as commissioner of health of a state or territory.

New York City

Dr. Tatum Gives Annual Lecture.—Edward L. Tatum, Ph.D., of Rockefeller Institute presented "Molecular Genetics—Microbes to Man?" as the John F. Anderson Memorial Lecture in Medicine at the University of Virginia School of Medicine, Charlottesville, Nov. 23. The lectureship was established in 1955.

Student Wins Honors Scholarship.—The Alumni Association of the State University of New York Downstate Medical Center in Brooklyn awarded its first Honors Scholarship to Mr. Michael Bromer, Brooklyn. A first-year medical student at the Downstate Medical Center, Mr. Bromer will receive up to $1,000 per year for each of his four years in medical school. The funds for the scholarship are provided by the Research Scholarship, Student Loan and Welfare Fund of the Alumni Association. The award was made in the Alumni Office at the Downstate Medical Center on Nov. 16 by Dr. Alfred P. Ingegno, Brooklyn, chairman of the board of trustees of the fund.

Dr. Ochoa Honored.—Dr. Severo B. Ochoa, a 1959 Nobel Laureate in Medicine, and chairman of the department of biochemistry, New York University College of Medicine, was given the New York University Medal at a reception at NYU–Bellevue Medical Center Nov. 20. The alumni of New York University also paid tribute to Dr. Ochoa at a luncheon on Nov. 19, when he was awarded the second honorary lifetime membership given to distinguished persons from New York University. The first honorary membership was given last year to Dr. Jonas E. Salk, Pittsburgh, 1939 graduate of the College of Medicine.

Personal.—Dr. Louis H. Bauer, chairman of the board of United Medical Service, New York's Blue Shield plan, announced his decision to retire. He will be succeeded by Dr. Carl R. Ackerman, president of the Bronx County Medical Society. Dr. Bauer, secretary-general of the World Medical

Association and former president of the American Medical Association, has headed the Blue Shield organization since 1954.—Dr. Alexander Brunschwig, who served as honorary professor at the University of Guayquil, Ecuador, was awarded the "Oficer de Order Al Merito" by the Republic of Ecuador, recently.

OHIO

Law-Medicine Institute.—The Law-Medicine Center of Western Reserve University, Cleveland, will offer a two-day institute, "The Back: A Law-Medicine Problem Reappraised," Feb. 12-13. A special feature of this institute will be two actual settlement negotiations in the afternoon session Feb. 13: one involving a whiplash case and the other a disc case. The morning sessions will be devoted to defining the back and studying in depth the function of the back and the relationship of the back to the whole body as well as studying what trauma and disease affect the back and how they affect it. Rehabilitative procedures, diagnosis and evaluation techniques to determine disabilities will be investigated. The institute will be held in the Hatch Auditorium of the Newton D. Baker Building on the Western Reserve University campus from 9 a. m. to 4:30 p. m. each day. The fee for this institute is $25. Housing facilities will be available. For registration or information, contact Mr. Oliver Schroeder Jr., the Law-Medicine Center, Western Reserve University, Cleveland 6.

OREGON

Dr. Weinzirl Receives Public Health Award.—Dr. Adolph Weinzirl, chairman of the department of public health and preventive medicine, University of Oregon Medical School, Portland, has received the Oregon Public Health Association annual award for 1959. Dr. Weinzirl received the plaque for his "outstanding contribution to the betterment of public health during his more than 30 years of service in this field."

TEXAS

Symposium on Cancer Research.—The University of Texas M. D. Anderson Hospital and Tumor Institute announces the 14th annual Symposium on Fundamental Cancer Research, "Cell Physiology of Neoplasia," to be held Feb. 25-27. Tao-Chiuh Hsu, Ph.D., head, section of experimental cytology, department of biology, M. D. Anderson Hospital, chairman of the symposium committee, outlined the general scope of the program, which includes morphology of cells, behavior of organelles, submicroscopic structures, cytochemistry, growth phenomena, and biochemical properties of cells. Each presentation will be followed by a 15-minute discussion period. Information may be obtained by writing: Editorial Office, The University of Texas M. D. Anderson Hospital, Texas Medical Center, Houston 25, Texas.

GENERAL

Dr. Candau Accepts Extension of Directorship.—Dr. M. G. Candau, Brazil, director-general of the World Health Organization, accepted the 12th World Health Assembly's offer to extend his term of office by three years. Dr. Candau was first elected WHO director general in 1953. His present directorship expires July 20, 1960. His acceptance of the assembly's offer will extend that date until July, 1963.

Publisher Buys Six Journals.—The president of the Reuben H. Donnelley Corporation, Chicago, announced the purchase of six publications from Drug Publications, Inc., New York City. The publications represented in the sale were *The American Journal of Medicine, The American Journal of Surgery, The American Journal of Clinical Nutrition, The American Journal of Cardiology, Modern Drug Encyclopedia and Therapeutic Guide,* and *The Veterinary Drug Encyclopedia.* The Donnelley Company, founded in 1886, began publishing magazines in 1931. The company's corporate offices are in the Prudential Building, Chicago.

Competition Open for Cancer Award.—The Ann Langer Cancer Research Foundation announced the third annual award of $500 "for meritorious investigation in the field of cancer research, either clinical or laboratory." The award is being supported by the family of the late Bertha Goldblatt Teplitz and carries her name. Competition is limited to physicians and other scientists, clinical or laboratory, under the age of 45. The name of the recipient of the 1960 award will be announced May 1. Nominations should be submitted to Teplitz Award Committee, 612 N. Michigan Ave., Chicago 11, no later than Feb. 1, 1960, and should be accompanied by a short one-page statement and biography.

Meeting on Forensic Pathology.—The second International Meeting of Forensic Pathology will be held in New York City Sept. 18-22. The meeting will include the dedication of the new building for the office of chief medical examiner of the City of New York, which is under construction and scheduled for completion in the early summer of 1960. The Commodore Hotel will serve as headquarters. Six half-day scientific sessions will be held at the New York University Post-Graduate Medical School. The meeting will have multiple sponsorship of scientific societies in this country and abroad concerned with forensic pathology and legal medicine. A banquet and other activities are planned. Following the completion of the sessions in New York, those in attendance are invited to Washington, D. C., to visit the Armed Forces Institute of Pathology, the Federal Bureau of Investigation, the Smithsonian Institute, and other places of interest. All inquiries may be addressed to Dr. Milton Helpern, 55 Eas End Ave., New York 28.

Report on Shooting Accidents.—Statisticians of the Metropolitan Life Insurance Company reported that about 2,400 persons were killed in shooting accidents of all kinds in 1958. Such accidents are frequent during the three-month period from October through December, with the peak in November, when hunting activities are at a maximum. Nine-tenths of the firearm accident victims are males, the statisticians point out, and adolescent boys are more frequently the victims than are members of any other age groups. Youths at ages 15-19 years, while comprising only 3% of the total population of the United States account for about 16% of those fatally injured in firearm accidents. Despite the frequency of hunting accidents, nearly half of the people killed in firearm accidents are injured in and about the home.

New Journal of Neurology.—In December the first issue of *International Journal of Neurology* appeared. Each number of the new journal will deal with one specific subject, and the first issue will be dedicated to epilepsy. The editorial and advisory board of this journal is composed of neurologists of countries of Europe and America, and the articles can be written in English, French, Spanish, and German, with a summary translated into the remaining languages. All the authors will collaborate by invitation. The second issue will be devoted to brain vascular diseases. The journal will appear every three months. Each number will be a symposium of the latest news in every field of neurology. The subscription rate is $10 a year, which can be sent to the following address: International Journal of Neurology, calle Buenos Aires 363, Montevideo, Uruguay.

Conference on Infertility.—The International Fertility Association will present a Pan American Conference on Infertility, at the Eden Roc Hotel, Miami Beach, Fla., Jan. 10-14. The program is arranged in eight sections as follows:

Female Surgery.
Female Diagnosis.
Male Infertility.
General, Somatic and Psychosomatic.
Ovum and Fertilization.
General Diagnosis and Therapy.
Progestins.
Educational Program.

Participants will represent England, Canada, Mexico, Cuba, France, and the United States. A round-table discussion on atomic radiation during the educational section will include Dr. Louis M. Orr, Orlando, Fla., President, American Medical Association, and Dr. Ross T. McIntire, Chicago, director International College of Surgeons. A social program is planned. The conference is acceptable for category II credit for members of the American Academy of General Practice. For information, write Dr. M. Leopold Brodny, 4646 Marine Drive, Chicago 40, associate secretary general, International Fertility Association.

Life Expectancy.—America's wage earners and their families registered a slight increase in average length of life last year, but still did not equal the all-time high recorded in 1956, it is reported by statisticians of the Metropolitan Life Insurance Company. Average length of life—or expectation of life at birth—among the Metropolitan's industrial policy holders was 70.1 years in 1958, or 0.1 year below the all-time high and an equal amount above the 1957 figure. Last year was the fourth in succession in which the average lifetime of these insured persons remained at about the 70-year mark. Prior to 1954, the increase in expectation of life at birth averaged about one-half year per annum. The average lifetime was only 34 years in 1879-1894; it rose to a little more than 50 years at the close of World War I, reached 60 years in 1935, and passed the 65-year mark in 1946. Since 1938 the average remaining lifetime at age 25 has increased 5.2 years. Even at age 45 the average has risen 3.7 years, and now is as much as 29.4 years.

Surgeons and Nurses Meeting in Boston.—Surgeons, nurses, and related medical personnel from throughout the country are invited to attend a comprehensive, four-day sectional meeting of the American College of Surgeons in Boston Feb. 29-March 3. Headquarters will be the Statler Hilton and Sheraton Plaza hotels, with many sessions scheduled at Boston hospitals. This meeting will include sessions in general surgery and separate programs in the surgical specialties for gynecologists and obstetricians, ophthalmic surgeons, orthopedic surgeons, otolaryngologists, thoracic surgeons, urologists, and nurses. This meeting is designed "to inform the medical profession at large about developments in surgery, and to focus attention on newer ways of handling problems encountered in daily practice." Dr. Claude E. Welch, clinical associate professor of surgery, Harvard Medical School, is chairman of the local advisory committee on arrangements. The nurses' program is the only one to be conducted by the college in 1960. Nurses from Canada and the U. S. are invited. For information, write the American College of Surgeons, 40 E. Erie St. Chicago 11.

Grants to Aid Medical Education.—Grants to medical education by the John and Mary R. Markle Foundation amounted to $920,000 during 1958-1959, it was announced in the annual report of the fund. The chief interest of the foundation continued to be support of young faculty members of medical schools in the United States and Canada, selected by the fund as Markle Scholars in Medical Science. The sum of $750,000 was allocated toward the support of 25 scholars in medical schools at the following colleges or universities: Chicago, Colorado, Columbia, Duke, Harvard, Johns Hopkins, Louisville, McGill, Miami, Montreal, New York Downstate (Brooklyn), North Carolina, Northwestern, Pennsylvania, Pittsburgh, Tulane, Utah, Vanderbilt, Vermont, University of Washington

(Seattle), Washington (St. Louis), Wayne State, Western Reserve, Wisconsin, and Yale. Each school was allotted $30,000 toward the scholar's support, $6,000 annually for five years. The largest single grant of the year, $100,000, was made to Dartmouth Medical School for general support. The hundredth anniversary of the birth of John Markle, Pennsylvania coal operator who established the fund, occurred during the year. The report reviews the work of the fund since it was established by Mr. Markle in 1927. Since then a total of $5,447,491 has been given for medical research, chiefly as grants-in-aid, $1,825,000 for medical and dental education, $7,579,000 for the Markle Scholar program, and $5,692,224 for welfare and other grants.

Society News.—Dr. Malcolm H. Merrill, Berkeley, Calif., was installed as president of the **American Public Health Association** during its 87th annual meeting, Oct. 19-23. Marion W. Sheahan, R.N., deputy general director of the National League for Nursing was chosen as president-elect to succeed Dr. Merrill. Elected as vice-presidents were Dr. Paulo Cesar de Azevedo Antunes, of Sao Paulo, Brazil; Dr. Jules A. Gilbert, Montreal; and Dr. Fred L. Soper, of Washington, D. C. Charles Glen King, Ph.D., New York City, was reelected treasurer.——Mr. Theodore Berland (2840 Berwyn, Chicago) was appointed public relations counselor to the **International College of Surgeons.**——The new officers of the **Southwestern Medical Association** elected at the annual meeting Nov. 5-7 are: Dr. Russell L. Deter, El Paso, president; Dr. Howard D. Cogswell, Tucson, president-elect; Dr. Brian S. Moynahan, Santa Fe., vice-president; and Dr. Merle D. Thomas, El Paso, secretary-treasurer. The 1960 meeting is scheduled to be held in El Paso but the date has not been selected.——The **American Rhinologic Society** has elected the following officers for 1959-1960: president, Dr. Roland M. Loring, Chicago; president-elect, Dr. Ivan W. Philpott, Denver; vice-president, Dr. Raymond L. Hilsinger, Cincinnati; secretary, Dr. Robert M. Hansen, Portland, Ore.; treasurer, Dr. George G. Fischer, Wilmette, Ill.; regional directors, Drs. Leland R. House, Los Angeles, Lewis E. Morrison, Indianapolis, and Amos E. Friend, Manchester, Conn.

Fellowships in Industrial Medicine.—The United States Atomic Energy Commission announced its Special Fellowships in Industrial Medicine for 1960-1961 administered by the Atomic Energy Project, School of Medicine and Dentistry, University of Rochester, New York. The fellowships provide advanced training and on-the-job experience in industrial medicine, particularly in relation to the atomic energy industry. The selection of fellows is made by the Atomic Energy Commission on recommendation of the Committee on Fellowships in Industrial Medicine. Eight fellowships will be available for 1960-1961. They are open to men and women physicians who are citizens of the United States and have graduated from an approved college of medicine at least two years prior to beginning tenure of the fellowship and who are licensed to practice medicine in a state or territory. Successful candidates will be required to have full F. B. I. background investigation. The training consists of (1) an academic year with lecture and laboratory instruction in the practice of industrial medicine, industrial hygiene, industrial toxicology, nuclear physics, biostatistics, and the public health aspects of occupational medicine; (2) an in-plant training year, in which the fellow will be assigned to one or more of the medical departments of the major operating plants and laboratories under the direction of the A. E. C. Applications for 1960-1961 should be filed before Jan. 1. Selection of fellows will be made on or before Feb. 1. The tenure of the fellowship will be arranged to begin about July 1 for a summer session or at the opening of the school in the fall. The stipend is $5,000; the sum of $350 is added for a wife and $350 more for each dependent child. Tuition and laboratory fees will be paid in academic courses. During the in-plant year the stipend is paid by the plant. Address all inquiries to the Atomic Energy Commission, Fellowships in Industrial Medicine, Atomic Energy Project, University of Rochester School of Medicine and Dentistry, Rochester 20, N. Y., Attn: Henry A. Blair, Ph.D.

Organization of Cancer Institute Directors.—The directors of cancer research institutes in America have formed the Association of Cancer Institute Directors for the purpose of exchanging information among the various institutes. The organizational meeting was held at Roswell Park Memorial Institute, Buffalo, N. Y. The organization is composed of the senior scientific executives of those institutions and autonomous divisions and departments whose principal activities are concerned with the study of malignant disease and the treatment of cancer patients. Officers elected at the first meeting held in October at Memorial Center for Cancer and Allied Diseases in New York City include: president, Dr. George E. Moore, director, Roswell Park Memorial Institute; vice-president, Dr. Sidney Farber, director of research, Children's Cancer Research Foundation, Boston; and secretary-treasurer, Dr. Randolph Lee Clark Jr., director, University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas. The association has been designed "to support investigations of the causes, nature, treatment, and prevention of malignant diseases, to encourage the exchange of ideas, information, personnel and special facilities between groups with predominant interests in cancer; to foster educational opportunities the biomedical sciences; to provide guidance to private and civil organizations concerning cancer research, education and the care of cancer patients; and to expedite the dissemination of information by the meeting together of the scientific executive officers of cancer institutes." The association will, in the future, consider members from among the scientific directors of cancer institutes of foreign countries.

LATIN AMERICA

Course in Reconstructive Nasal Surgery.—An international course, "The Fundamentals of Reconstructive Surgery of the External Nasal Pyramid and the Nasal Septum," will be presented in Mexico City, July 4-5, under the auspices of the Escuela Nacional de Medicina e Division del Doctorado, and with the cooperation of the American Rhinologic Society. The guest professor will be Dr. Maurice H Cottle, professor of otolaryngology, Chicago Medical School, and founder of the American Rhinologic Society. Dr. Cottle will be assisted by a faculty of specialists from the United States and Mexico. Lectures will be presented simultaneously in English and Spanish. Applicants for the course must be diplomates of the American Board of Otolaryngology, or have equivalent status. For information, write Dr. Robert M. Hansen, secretary of the American Rhinologic Society, 1735 N. Wheeler Ave., Portland 12, Ore.

FOREIGN

Psychotherapy Week in Lindau, Bavaria.—The 10th Lindau Psychotherapy Week will take place in Lindau, Bavaria, May 2-7. The main theme of the lectures and seminars will be group psychotherapy. There will also be lectures and guided tours through an exhibition in which paintings, sculptures, and other arts and crafts will be shown which were done in the course of psychotherapy. The language of the meeting will be German. For information, write the Secretarial Office, Lindau Psychotherapy Week, Munich 2, Dienerstrasse 17.

CORRECTION

Strongyloidiasis.—In a foreign letter from Brazil, entitled "Strongyloidiasis," appearing in The Journal, Nov. 21, page 1723, the words "with dithiazanine iodide" were inadvertently dropped from the end of the first sentence.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, June 24. Final date for filing application is January 10. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Oral.* San Francisco, March 30-April 1; New York City, Nov. 14-17. Closing date for filing application is Jan. 2 and July 1. *Written.* Oct. 17. Closing date for filing application is May 1. *Oral. Gastroenterology.* Philadelphia, March 11-12. Final date for filing application is January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: *Part I, Written.* Chicago, January 16. Candidates notified of their eligibility to participate in the Part I examination must submit their case abstracts within thirty days of notification of eligibility. *Part II, Oral.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications was Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral,* Chicago, Oct. 3-7. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pediatrics: *Written.* Jan. 8. Final date for filing application for the written examination was Dec. 1. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Milwaukee, May 1960. Final date for filing application is January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Psychiatry and Neurology: San *Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959.* Sec., Dr. David A. Boyd, 102-110 Second Ave S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Cincinnati, Spring 1960. Deadline for filing applications is Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Oral Examinations (Part II):* Winston-Salem, No. Car., Jan. 18-19; New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, Feb. 12. Final date for filing application was Dec. 1. *Oral.* May 1960. Final date for filing application was Dec. 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

ARMY

Colonel Glass Receives Award.—Col. Albert J. Glass, chief psychiatry and neurology consultant to the surgeon general, received the Gorgas award for his role in the development of preventive psychiatry. The award, consisting of a silver medallion, a citation, and $500, was presented during the annual dinner of the Association of Military Surgeons in Washington. The award is made by Wyeth Laboratories in memory of Surgeon General William C. Gorgas, whose work in controlling yellow fever made possible the construction of the Panama Canal.

NAVY

Admiral Cooper Honored.—Vice-adm. Thomas F. Cooper, M. C., U. S. Navy, retired, was presented the Founder's medal by the Association of Military Surgeons at the annual convention in Washington, D. C., in November. This award, consisting of a scroll and a life membership in the association, was given for outstanding contribution to military medicine and for meritorious service to the association.

VETERANS ADMINISTRATION

Award to Dr. Cummings.—The Veterans Administration's exceptional service award was presented in October to Dr. Martin M. Cummings, director of medical research for the VA. The VA award was in recognition of distinguished contributions to medical research in the agency.

Personal.—Dr. Marc J. Musser, formerly director of professional services at the Houston, Texas, Veterans Administration hospital, was appointed director of medical research for the VA in Washington, D. C. In his new position he will coordinate a nationwide program of some 6,000 individual and cooperative studies, with major categories in cancer, cardiovascular disease, mental illness, aging, tuberculosis, atomic medicine, and dental health.

PUBLIC HEALTH SERVICE

Clinical Center Studies.—The cooperation of physicians in nearby areas is requested in a study of carcinoma of the thyroid and of chondrosarcoma. These studies are being conducted by the radiation branch of the National Cancer Institute in the Clinical Center of the National Institutes of Health, Bethesda, Md. The primary purpose of the first is a search for therapeutic methods which may favorably affect the course of this disease. This study has three major components. The first two components are concerned with the relationships of structure and function of tumor components to hormonal influences and to the uptake of radioactive iodine. The third is related to the study, development, and detection of autoimmune antibodies developed to the patient's own thyroid, thyroid cancer as the antigen, and the possible response of thyroid cancer to this antigen. Patients appropriate to this program are those in whom the diagnosis of cancer of the thyroid is established, whether or not they have had prior treatment.

The primary purpose of the second study is to determine the possible effects of large doses of radioactive sulfur on patients with chondrosarcoma. Recent studies at the clinical center have shown that the uptake of sulfur-35 by chondrocytes and the ground substance of the cellular and cartilaginous components of chondrosarcoma is higher by factors of 10 or more than the uptake in other human tissues. It is possible, therefore, that the uptake of sulfur-35 by chondrosarcoma might be sufficient to put the radiation dose within the range of therapeutic effect on this tumor. It is known, however, from the previous studies mentioned that such doses have a severely depressive effect on hematopoiesis and, as an additional part of the study, this effect and means of preventing it are being investigated. Patients accepted for this study are those with inoperable chondrosarcoma but with a tumor located where it is accessible for biopsy so that the sulfur-35 content can be analyzed.

Patients for either study should not be in the terminal phase of the disease, since such a circumstance allows no follow-up period for the determination of results. Accepted patients will be studied for various periods of time and their progress may be followed subsequently by either the referring physician or physicians at the clinical center. A comprehensive and individual program will be instituted for each patient and will include appropriate supportive and symptomatic care as well as the experimental therapeutic study described above. Physicians interested in the possibility of referring such patients should write or telephone: Charles G. Zubrod, M.D., clinical director, National Cancer Institute, Bethesda 14, Md. (OLiver 6-4000, ext. 4346), or J. Robert Andrews, M.D., chief, radiation branch, National Cancer Institute, Bethesda 14, Md. (OLiver 6-4000, ext. 3351).

Personal.—Dr. C. K. Himmelsbach was appointed associate director of the clinical center, the combined clinical and laboratory research facility of the National Institutes of Health, Bethesda, Md. He succeeds the late Dr. Kenneth W. Chapman.

DEATHS

Baskin, Charles Llewelyn, Raleigh, N. C.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1912; died Sept. 19, aged 76.

Benzenberg, Henry Carl Ⓜ Selinsgrove, Pa.; Long Island College Hospital, Brooklyn, 1944; interned at the Englewood (N. J.) Hospital; served a residency at the Woman's Hospital and Doctors Hospital in New York City; member of the American Academy of General Practice; president-elect of the Susquehanna Valley Heart Association; veteran of World War II; recalled to active duty in the U. S. Naval Reserve in January, 1953, and relieved from duty in December, 1954; died Sept. 21, aged 40.

Bettison, William Leslie Ⓜ Grand Rapids, Mich.; University of Michigan Medical School, Ann Arbor, 1922; member of the American College of Gastroenterology; veteran of World Wars I and II; on the honorary staff of Blodgett Memorial Hospital, where he died Sept. 19, aged 63.

Blotz, B. Franklin Ⓜ Rocky Ford, Colo.; Jefferson Medical College of Philadelphia, 1914; past-president of the Colorado State Board of Medical Examiners; past-president of the board of education; on the staff of the Pioneers Memorial Hospital; veteran of World War I; died in the Veterans Administration Hospital, Denver, Sept. 25, aged 70.

Burden, John Gerard Ⓜ Glendale, Wis.; University of Michigan Medical School, Ann Arbor, 1943; interned at the Baptist Memorial Hospital in Memphis, Tenn.; formerly a resident at the Hospital for Special Surgery in New York City; on the staffs of the Memorial Hospital and St. Michael Hospital in Milwaukee, where he died Sept. 24, aged 41.

Burke, John Woolfolk Ⓜ Washington, D. C.; University of Virginia Department of Medicine, Charlottesville, 1906; specialist certified by the American Board of Ophthalmology; member of the American Ophthalmological Society, of which he was past-president, and the Association for Research in Ophthalmology; veteran of World War I; cited for serving for more than 30 years at Episcopal Eye, Ear and Throat Hospital, now a part of Washington Hospital Center, and received a gold-headed cane; formerly on the faculty of Georgetown University School of Medicine; died in the Doctors Hospital Oct. 5, aged 75.

Carpenter, John Leland Ⓜ Alexandria, Ind.; Indiana University School of Medicine, Indianapolis, 1928; interned at the Methodist Episcopal Hospital in Indianapolis; died in the Ball Memorial Hospital, Muncie, Sept. 22, aged 59.

Cohn, Hans Ferdinand Joachim, Cleveland; Friedrich-Wilhelms-Universitat Medizinische Fakultat, Berlin, Germany, 1914; died Sept. 2, aged 72.

Cunningham, Michael Angelo Ⓜ Beaumont, Texas; John A. Creighton Medical College, Omaha, 1913; member of the American College of Chest Physicians and the American Trudeau Society; superintendent of the Jefferson County Tuberculosis Hospital; medical director of the Beaumont Tuberculosis Association; served as medical director of the Holy Cross (N. M.) Sanatorium; died Sept. 20, aged 70.

Draper, Arthur Derby Ⓜ Tampa, Fla.; Harvard Medical School, Boston, 1903; died in St. Joseph's Hospital Sept. 26, aged 85.

Eaton, John Parker, Rusk, Texas; University of Arkansas School of Medicine, Little Rock, 1941; interned at the St. Vincent's Infirmary in Little Rock, Ark.; veteran of World War II; died Sept. 24, aged 51.

Eller, Warren Herbert Ⓜ Sayville, N. Y.; University of Nebraska College of Medicine, Omaha, 1923; member of the American Academy of General Practice; died Sept. 30, aged 63.

Ewald, August Ludwig Jr. Ⓜ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1935; veteran of World War II; served an internship and residency at the Maryland General Hospital, where he was a member of the staff, and where he died, Sept. 20, aged 52.

Fall, Hugh Vincent Ⓜ Roswell, N. M.; Toledo Medical College, 1907; past-president of the New Mexico Medical Society and of the Chaves County Medical Society; veteran of World War I; on the staffs of St. Mary's Hospital and the Eastern New Mexico Medical Center; died Sept. 18, aged 76.

Field, Merton, Chippewa Falls, Wis.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; died Sept. 17, aged 88.

Fiman, Charles Elden, Madison, Tenn.; College of Medical Evangelists, Loma Linda and Los Angeles, 1938; member of the American Psychiatric Association; on the staff of the Madison Sanitarium and Hospital; died Sept. 26, aged 53.

Ⓜ Indicates Member of the American Medical Association.

Finch, Rollac Dean Ⓜ Flora, Ill.; St. Louis University School of Medicine, 1912; on the staff of the Clay County Hospital, where he died Sept. 22, aged 72.

Frybarger, Clarence Edward, Andrews, Ind.; Chicago College of Medicine and Surgery, 1916; veteran of World War I; served on the staff of the Oak Park (Ill.) Hospital for many years; died in the Huntington County Hospital, Huntington, Sept. 21, aged 70.

George, William Wellington Ⓜ West Palm Beach, Fla.; Georgetown University School of Medicine, Washington, D. C., 1922; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; member of the American College of Cardiology; fellow of the American College of Physicians; veteran of World War I; associated with St. Mary's and Good Samaritan hospitals; died Sept. 30, aged 61.

Gerchow, Keith Elmer Ⓜ Morgantown, W. Va.; born in Fairmont, Aug. 16, 1911; University of Georgia School of Medicine, Augusta, 1937; interned at the Chesapeake and Ohio Railway Hospital in Huntington, W. Va.; served a residency at the Gill Memorial, Eye, Ear and Throat Hospital in Roanoke, Va.; member of the Southeastern Surgical Association; past-president of the Monongalia County Medical Society; past-secretary of the West Virginia Otolaryngology Society; veteran of World War II; served on the staff of the Beckley (Va.) Hospital; died in the Monongalia General Hospital Sept. 22, aged 48.

Giere, Ellis Karl Ⓜ Auburn, Wash.; University of Minnesota Medical School, Minneapolis, 1930; member of the American Academy of General Practice; on the staff of the Auburn General Hospital, where he died Sept. 29, aged 54.

Harris, Robert Locke Ⓜ Odessa, Texas; Baylor University College of Medicine, Dallas, 1920; veteran of World War I; died Sept. 19, aged 65.

Hegele, Herbert William, Portland, Ore.; Rush Medical College, Chicago, 1899; died in the Providence Hospital Sept. 19, aged 81.

Hoggard, William Alden Ⓜ Woodville, N. C.; University College of Medicine, Richmond, 1907; Vanderbilt University School of Medicine, Nashville, Tenn., 1914; died Sept. 24, aged 77.

Johnston, Robert Miller Ⓜ New Kensington, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1911; veteran of World War I; past-president of Citizens General Hospital staff, where he was the resident physician; died Sept. 21, aged 81.

Jones, John William Ⓜ Pottsville, Pa.; born in Cartersville, Ga., Feb. 7, 1903; Emory University School of Medicine, Atlanta, 1927; specialist certified by the American Board of Radiology; member of the Radiological Society of North America; fellow of the American College of Radiology; served as president of the Schuylkill County Medical Society; past-president of the Schuylkill County unit of the American Cancer Society; a director of the Tuberculosis and Health Society of Pottsville; veteran of World War II; associated with the Pottsville Hospital, where he died Sept. 24, aged 56.

Knowlton, William Amherst Jr., Cleveland; University of Wooster Medical Department, Cleveland, 1895; for many years physician and surgeon for the Baltimore & Ohio Railroad; on the staff of St. Alexis Hospital; died Sept. 19, aged 88.

Kovach, John Stephen Ⓜ Cleveland; St. Louis University School of Medicine, 1930; during World War II served in the U. S. Coast Guard, U. S. Public Health Service; on the staff of the Polyclinic Hospital; died in the Lakeside unit of the University Hospitals Sept. 21, aged 53.

Kramer, Frederic Carl, Phoenix, Ariz.; University of Nebraska College of Medicine, Omaha, 1959; veteran of World War II; intern at the Maricopa County General Hospital; died Aug. 24, aged 35.

Leavy, Philip Gerard Ⓜ Pittsburgh; Georgetown University School of Medicine, Washington, D. C., 1934; member of the American College of Cardiology; veteran of World War II; on the faculty of the University of Pittsburgh School of Medicine; on the staffs of the St. Francis Hospital and the Pittsburgh Hospital, where he died Sept. 26, aged 52.

Leeds, Alexander Bartholomew, Albuquerque, N. M.; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1902; specialist certified by the American Board of Internal Medicine; member of the American Psychosomatic Society; fellow of the American College of Physicians; for many years practiced in Chickasha, Okla.; on the staff of the St. Joseph Sanatorium and Hospital; died in the Presbyterian Hospital Sept. 17, aged 82.

LeFevre, Walter Irwin, Cleveland Heights, Ohio; Bellevue Hospital Medical College, New York City, 1897; died in St. Augustine, Fla., Sept. 22, aged 85.

Lester, Frank Marvin Ⓜ New York City; Howard University College of Medicine, Washington, D. C., 1949; interned at the Freedmen's Hospital in Washington, D. C., where he served a residency; served a residency at the Lincoln Hospital; specialist certified by the American Board of Obstetrics and Gynecology; certified by the National Board of Medical Examiners; veteran of World War II; served in the U. S. Naval Reserve; died in the Hospital for Joint Diseases Sept. 17, aged 36.

Loughmiller, Robert Farris Ⓜ Oklahoma City, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1937; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; flight surgeon with the rank of colonel in the U. S. Army from 1938 to 1944; on the staffs of St. Anthony's and Mercy hospitals; died Sept. 22, aged 46.

McCready, James Homer Ⓜ Pittsburgh; born Feb. 18, 1882; Jefferson Medical College of Philadelphia, 1906; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; for many years on the faculty of the University of Pittsburgh School of Medicine, where he was professor emeritus of otolaryngology; president emeritus of the medical staff, Eye and Ear Hospital; on the senior staffs, University Health Center, St. Francis Hospital, and Sewickley, (Pa.) Valley Hospital; died Sept. 28, aged 77.

McIntire, Erastus Clark Ⓜ Hurricane, Utah; University of Louisville (Ky.) School of Medicine, 1926; veteran of World War I; served on the staffs of the Iron County Hospital in Cedar City and the Dixie Memorial Hospital in St. George; died Sept. 4, aged 61.

MacLeod, Emily Clark, Chattanooga, Tenn.; Tufts College Medical School, Boston, 1913; for many years practiced in Boston; died Sept. 25, aged 81.

Madden, Leon Irving Ⓜ Avon, Conn.; Harvard Medical School, Boston, 1910; died in Haverhill, N. H., Sept. 19, aged 76.

Means, Frank M. Ⓜ Holyoke, Colo.; Lincoln (Neb.) Medical College of Cotner University, 1903; died in the Phillips County Hospital Sept. 26, aged 83.

Merillat, Irene Socialista Ⓜ El Monte, Calif.; Loyola University School of Medicine, Chicago, 1925; on the staff of the Behrens Memorial Hospital in Glendale; died in Glendale Sept. 25, aged 61.

Norton, Arthur Holmes, Eugene, Ore.; University of Michigan Homeopathic Medical School, Ann Arbor, 1904; specialist certified by the American Board of Ophthalmology; for many years a medical missionary in Korea; on the staff of the Eugene Hospital and Clinic; died Sept. 28, aged 81.

Oakes, Charles Gratton Ⓜ Sapulpa, Okla.; University of Kansas School of Medicine, Kansas City, 1934; interned at St. Joseph Hospital in Kansas City, Mo.; served on the staffs of the Hillcrest Hospital in Tulsa and the Bartlett Memorial Hospital in Sapulpa; died in Tulsa Sept. 25, aged 50.

O'Brien, Raymond Wilson Ⓜ Kansas City, Mo.; University of Kansas School of Medicine, Kansas City, Kan., 1943; interned at the University of Kansas Hospitals in Kansas City, Kan.; served a fellowship at the Mayo Foundation in Rochester, Minn., and residency at the Henry Ford Hospital in Detroit; on the staffs of the St. Luke's and the Kansas City General hospitals; died Sept. 29, aged 42.

Otto, Frank Wesley Ⓜ Los Angeles; born in Great Bend, Kan., March 28, 1892; College of Physicians and Surgeons, Los Angeles, 1921; emeritus assistant clinical professor of medicine, University of Southern California School of Medicine; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-member of council, Los Angeles County Medical Association, of which he was chairman of the board of trustees; honorary life member of the Hollywood Academy of Medicine; life member and past-president of the University of Southern California General Alumni Association; twice president of the California Board of Medical Examiners; chief of the Division of Private Institutions for the California Department of Mental Hygiene; on the senior attending staff, California Hospital, where he died Sept. 23, aged 67.

Penn, Frank Hogan Jr. Ⓜ Mullens, W. Va.; Medical College of Virginia, Richmond, 1932; interned at St. Mary's Hospital in Huntington, W. Va.; served as president of the Wyoming County Medical Society; died Sept. 24, aged 50.

Rush, John Alfred, Miami, Fla.; Emory University School of Medicine, Atlanta, 1957; interned at the Grady Memorial Hospital in Atlanta, Ga.; served a residency at the Jackson Memorial Hospital, where he died Sept. 19, aged 29.

Rogers, James Rufus, New Orleans; Tulane University School of Medicine, New Orleans, 1948; interned at Charity Hospital of Louisiana in New Orleans, where he served a residency; served a residency at the Prospect Heights Hospital in Brooklyn and St. Mary's Hospital and Sanatorium in Tucson, Ariz.; died in the Emory University Hospital, Atlanta, Sept. 21, aged 35.

Seidman, Julius Ⓜ Los Angeles; born in Winthrop, Mass., June 14, 1915; Northwestern University Medical School, Chicago, 1940; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; interned at Franklin Hospital in San Francisco and St. Louis City Hospital; served a residency at Bellevue Hospital in New York City; veteran of World War II; clinical instructor in psychiatry at the University of California School of

Medicine; since 1948 connected with the U. S. Veterans Administration; assistant chief in psychiatry at the Brentwood Hospital; died in the Wadsworth Hospital Sept. 29, aged 44.

Sparks, Edward Nathan, Remsen, N. Y.; University of the City of New York Medical Department, New York City, 1895; served as coroner of Remsen; died in Syracuse Sept. 24, aged 85.

Stearns, Albert Warren Ⓢ Billerica, Mass.; born in Billerica Jan. 26, 1885; Tufts College Medical School, Boston, 1910; for many years professor of psychiatry and dean at his alma mater, where he was dean emeritus; served as head of the department of sociology in the Tufts College of Liberal Arts; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychiatric Association, New England Society of Psychiatry, and the American Academy of Arts and Sciences; past-president of the Boston Society of Psychiatry and Neurology and the Massachusetts Psychiatric Society; past-vice-president of the Massachusetts Medical Society; served as special investigator for the National Committee for Mental Hygiene in the survey of Arkansas, medical director, Massachusetts Society for Mental Hygiene, and psychiatrist at the Massachusetts State Prison; commissioner of correction, State of Massachusetts from 1929 to 1933; associate commissioner, department of mental diseases, from 1935 to 1938; veteran of World Wars I and II; for many years president of the Billerica Historical Society; past-president of the Bay State Historical League; at various times member of the Billerica School Committee, Billerica Board of Selectman, and Moderator of the Billerica Town Meeting; captain, M. C., U. S. Naval Reserve, retired; chief of neurology service, Boston Dispensary, from 1921 to 1945; consultant at the U. S. Naval Hospital in Chelsea from 1923 to 1929; consultant, Charles Choate Memorial Hospital in Woburn and St. Elizabeth's Hospital in Boston; in 1915 received a gold medal at the Panama Pacific Exposition; in 1943 recipient of an honorary doctor of science degree from his alma mater; author of "Personality of Criminals"; died Sept. 24, aged 74.

Stephens, Hiram Aubrey, Ponce de Leon, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1916; died in Pensacola Sept. 15, aged 69.

Tillery, Bert Ⓢ Columbus, Ga.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; veteran of World War I; on May 14, 1956, his friends honored him with a portrait which was unveiled at St. Francis Hospital, where he was first president and for many years member of the medical staff, and where he died Sept. 21, aged 71.

Thomason, James Archibald Ⓢ Fountain Inn, S. C.; University of Maryland School of Medicine, Baltimore, 1910; vice-president of the Citizens Bank; died in the Greenville (S. C.) General Hospital Sept. 25, aged 72.

Truax, Jesse P. Ⓢ Major, U. S. Army, retired, Lompoc, Calif.; Medical Department of Omaha University, 1897; entered the regular Army in 1918 and retired June 4, 1920, for disability in line of duty; served as resident physician at the Celite Company Hospital; died in San Luis Obispo Sept. 16, aged 86.

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Watson, Carl L., Falmouth, Mass.; College of Physicians and Surgeons, Boston, 1907; died in the New England Baptist Hospital, Boston, Sept. 26, aged 87.

Wilkinson, Charles Fore Jr., New York City; born in College Park, Ga., March 30, 1912; Emory University School of Medicine, Atlanta, 1937; interned at the University Hospital in Ann Arbor, Mich., where he served a residency; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians and the American Association for the Advancement of Science; member of the American Federation for Clinical Research, American Society of Human Genetics, American Society of Genetics, American Heart Association, Harvey Society, Society of Experimental Biology in Medicine, Society for Biological Research, and Sigma Xi; served as vice-president of the American Society for the Study of Arteriosclerosis; on Nov. 5, 1952, delivered the 36th Mellon lecture before the Society for Biological Research of the School of Medicine, University of Pittsburgh; professor and chairman of the department of medicine, New York University Post Graduate Medical School; formerly assistant professor of internal medicine and coordinator of graduate medical education, University of Michigan Medical School in Ann Arbor; in 1948-1949 associate director of the division of medicine at the W. K. Kellogg Foundation in Battle Creek, Mich.; visiting physician and director of the fourth (New York University) medical service, Bellevue Hospital, and of medical service, University Hospital; veteran of World War II and held the Bronze Star Medal; died in Westport, Conn., Sept. 29, aged 47.

Loughmiller, Robert Farris Ⓜ Oklahoma City, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1937; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; flight surgeon with the rank of colonel in the U. S. Army from 1938 to 1944; on the staffs of St. Anthony's and Mercy hospitals; died Sept. 22, aged 46.

McCready, James Homer Ⓜ Pittsburgh; born Feb. 18, 1882; Jefferson Medical College of Philadelphia, 1906; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; for many years on the faculty of the University of Pittsburgh School of Medicine, where he was professor emeritus of otolaryngology; president emeritus of the medical staff, Eye and Ear Hospital; on the senior staffs, University Health Center, St. Francis Hospital, and Sewickley, (Pa.) Valley Hospital; died Sept. 28, aged 77.

McIntire, Erastus Clark Ⓜ Hurricane, Utah; University of Louisville (Ky.) School of Medicine, 1926; veteran of World War I; served on the staffs of the Iron County Hospital in Cedar City and the Dixie Memorial Hospital in St. George; died Sept. 4, aged 61.

MacLeod, Emily Clark, Chattanooga, Tenn.; Tufts College Medical School, Boston, 1913; for many years practiced in Boston; died Sept. 25, aged 81.

Madden, Leon Irving Ⓜ Avon, Conn.; Harvard Medical School, Boston, 1910; died in Haverhill, N. H., Sept. 19, aged 76.

Means, Frank M. Ⓜ Holyoke, Colo.; Lincoln (Neb.) Medical College of Cotner University, 1903; died in the Phillips County Hospital Sept. 26, aged 83.

Merillat, Irene Socialista Ⓜ El Monte, Calif.; Loyola University School of Medicine, Chicago, 1925; on the staff of the Behrens Memorial Hospital in Glendale; died in Glendale Sept. 25, aged 61.

Norton, Arthur Holmes, Eugene, Ore.; University of Michigan Homeopathic Medical School, Ann Arbor, 1904; specialist certified by the American Board of Ophthalmology; for many years a medical missionary in Korea; on the staff of the Eugene Hospital and Clinic; died Sept. 28, aged 81.

Oakes, Charles Gratton Ⓜ Sapulpa, Okla.; University of Kansas School of Medicine, Kansas City, 1934; interned at St. Joseph Hospital in Kansas City, Mo.; served on the staffs of the Hillcrest Hospital in Tulsa and the Bartlett Memorial Hospital in Sapulpa; died in Tulsa Sept. 25, aged 50.

O'Brien, Raymond Wilson Ⓜ Kansas City,
University of Kansas School of Medicine, Ka
City, Kan., 1943; interned at the University
Kansas Hospitals in Kansas City, Kan.; serve
fellowship at the Mayo Foundation in Roche
Minn., and residency at the Henry Ford Hosp
in Detroit; on the staffs of the St. Luke's and
Kansas City General hospitals; died Sept.
aged 42.

Otto, Frank Wesley Ⓜ Los Angeles; born in G
Bend, Kan., March 28, 1892; College of Physic
and Surgeons, Los Angeles, 1921; emeritus assis
clinical professor of medicine, University of So
ern California School of Medicine; specialist c
fied by the American Board of Internal Medic
fellow of the American College of Physici
past-member of council, Los Angeles County M
ical Association, of which he was chairman of
board of trustees; honorary life member of
Hollywood Academy of Medicine; life member
past-president of the University of Southern C
fornia General Alumni Association; twice presi
of the California Board of Medical Exami
chief of the Division of Private Institutions fo
California Department of Mental Hygiene; or
senior attending staff, California Hospital, w
he died Sept. 23, aged 67.

Penn, Frank Hogan Jr. Ⓜ Mullens, W. Va.;
ical College of Virginia, Richmond, 1932; int
at St. Mary's Hospital in Huntington, W.
served as president of the Wyoming County
ical Society; died Sept. 24, aged 50.

Rush, John Alfred, Miami, Fla.; Emory Uni
School of Medicine, Atlanta, 1957; interned
Grady Memorial Hospital in Atlanta, Ga.;
a residency at the Jackson Memorial H
where he died Sept. 19, aged 29.

Rogers, James Rufus, New Orleans; Tular
versity School of Medicine, New Orleans
interned at Charity Hospital of Louisiana
Orleans, where he served a residency;
residency at the Prospect Heights Hosp
Brooklyn and St. Mary's Hospital and San
in Tucson, Ariz.; died in the Emory Un
Hospital, Atlanta, Sept. 21, aged 35.

Seidman, Julius Ⓜ Los Angeles; born in Wi
Mass., June 14, 1915; Northwestern Un
Medical School, Chicago, 1940; specialist
by the American Board of Psychiatry an
rology; member of the American Psychiatri
ciation; interned at Franklin Hospital in Sa
cisco and St. Louis City Hospital; served
dency at Bellevue Hospital in New York C
eran of World War II; clinical instructor
chiatry at the University of California S

Medicine; since 1948 connected with the U. S. Veterans Administration; assistant chief in psychiatry at the Brentwood Hospital; died in the Wadsworth Hospital Sept. 29, aged 44.

Sparks, Edward Nathan, Remsen, N. Y.; University of the City of New York Medical Department, New York City, 1895; served as coroner of Remsen; died in Syracuse Sept. 24, aged 85.

Stearns, Albert Warren Ⓜ Billerica, Mass.; born in Billerica Jan. 26, 1885; Tufts College Medical School, Boston, 1910; for many years professor of psychiatry and dean at his alma mater, where he was dean emeritus; served as head of the department of sociology in the Tufts College of Liberal Arts; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychiatric Association, New England Society of Psychiatry, and the American Academy of Arts and Sciences; past-president of the Boston Society of Psychiatry and Neurology and the Massachusetts Psychiatric Society; past-vice-president of the Massachusetts Medical Society; served as special investigator for the National Committee for Mental Hygiene in the survey of Arkansas, medical director, Massachusetts Society for Mental Hygiene, and psychiatrist at the Massachusetts State Prison; commissioner of correction, State of Massachusetts from 1929 to 1933; associate commissioner, department of mental diseases, from 1935 to 1938; veteran of World Wars I and II; for many years president of the Billerica Historical Society; past-president of the Bay State Historical League; at various times member of the Billerica School Committee, Billerica Board of Selectman, and Moderator of the Billerica Town Meeting; captain, M. C., U. S. Naval Reserve, retired; chief of neurology service, Boston Dispensary, from 1921 to 1945; consultant at the U. S. Naval Hospital in Chelsea from 1923 to 1929; consultant, Charles Choate Memorial Hospital in Woburn and St. Elizabeth's Hospital in Boston; in 1915 received a gold medal at the Panama Pacific Exposition; in 1943 recipient of an honorary doctor of science degree from his alma mater; author of "Personality of Criminals"; died Sept. 24, aged 74.

Stephens, Hiram Aubrey, Ponce de Leon, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1916; died in Pensacola Sept. 15, aged 69.

Tillery, Bert Ⓜ Columbus, Ga.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; veteran of World War I; on May 14, 1956, his friends honored him with a portrait which was unveiled at St. Francis Hospital, where he was first president and for many years member of the medical staff, and where he died Sept. 21, aged 71.

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In view of the fact that advanced diabetic retinopathy is regarded as a hopeless condition a therapeutic trial seems justified, since no great risk is taken. Therefore only patients with marked impairment of sight were treated with partial hypophysectomy. Follow-up examination of 10 of the patients ranged from six weeks to five and one-half months. In eight the vision remained unchanged. In these patients extensive degenerative plaques and hemorrhages in the fundus of the eye were noted and in some advanced proliferating retinitis was present. Two patients, whose predominant symptoms were hemorrhages and who had only few white foci in the fundus of the eye, showed some improvement of vision three to four months after operation.

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Poisoning in Children.—M. Berheim and co-workers (*Annales de médecine légale*, vol. 39, 1959) stated that of 13,000 children under 15 years of age treated in the pediatric clinic in Lyon, (1951-1958), there were 85 with cases of poisoning. Of these, 22 were caused by the accidental ingestion of drugs, 27 by other toxic substances, and 36 by side-effects of the prescribed therapy. Of the total number, 11 occurred in the first year of life and 21 in children under 4 years of age. Twelve of the patients died. The cause of death was toxicity of cortisone in three patients, of antibiotics in seven, of a barbiturate in one, and of basic aluminium salicylate in one. In 24 of the 36 patients who suffered from untoward side-effects the diagnosis was not established by the first physician treating the patient. In three infants a convulsive state was observed less than 10 minutes after the intramuscular administration of Bronchocilline. Choleriform syndromes were observed after the oral administration of chloramphenicol (one patient), chlortetracycline (one patient), and tetracycline (2 patients). All four patients died. In two patients with malignant hemorrhagic varicella, complications due to cortisone were fatal. Acidosis developed in two infants who received from 7 to 10 tablets of aluminium salicylate and died. Children are very sensitive to chlorpromazine, which caused pseudoencephalitic coma in two patients.

Transplantation of Kidney.—J. Hamburger and co-workers (*Presse méd.* Oct. 12, 1959, pp. 1771-1775) stated that survival of a transplanted kidney requires close kinship between recipient and donor, a long history of progressive uremia in the recipient, preoperative radiotherapy, and avoidance of any factor that might activate the immunological response such as blood transfusions or skin grafts even from the donor. They performed such a transplant on a 37-year-old man who was admitted to the hospital in April with advanced renal insufficiency of eight years duration. His general condition was only fair. It was decided to transplant a kidney from his brother who was a heterozygous twin. A skin graft from the patient to the donor taken during the operation was rejected by the donor on the 25th day after the transplant. This delayed rejection indicated close kinship. Furthermore a study of leukocytic antigens of the brothers showed only one disagreement in nine serologic tests.

The patient received preoperative irradiation with radioactive cobalt. The transplant was performed in June on the day after the second irradiation. The removal of the donor's kidney and the transplantation were performed in two adjoining operating rooms. The donor was under hypothermia at 29 C to increase the resistance of the transplant to the anoxic period of the transplantation. The left kidney taken from the donor was laid in the right iliac fossa of the recipient. The operation lasted 2 hours and 40 minutes for the donor and 4 hours and 30 minutes for his twin.

In the first 15 postoperative days there was satisfactory renal function with 1,800 ml. of urine per day containing 22.5 Gm. of urea per liter instead of 6 Gm. as observed before the operation. The blood urea level returned to normal. Between the 15th and the 21st day a real crisis in the renal function occurred with a decrease in urine volume and increase in blood urea. On the 21st day the urea clearance was 6 ml. per minute, on the 22nd day there was a rapid improvement with a urea clearance rate of 20 ml. per minute, and 73 days after the operation the proteinuria had disappeared. Four months after the transplant, the patient's general condition was excellent. The arterial pressure, which had temporarily climbed to 190/110 mm. Hg, was 140/90 mm. Hg. The authors believed that the critical postoperative period observed was due to an immunological reaction.

Gamma Globulin for Asthma in Adults.—At the Société Médicale des Hôpitaux de Paris, M. R. Benda and co-workers reported a series of 31 patients who had asthma, 24 of whom they treated with gamma globulin alone and 7 of whom received gamma globulin plus a protective serum. In the first group, 15 patients were improved, 8 showed no improvement, and in 1 the condition was aggravated. In the second group five were improved. Of the 20 patients who improved, 3 had recurrences after a few weeks. In the other 17 the improvement was permanent. The increase in serum protective power was less marked with gamma globulin alone than when it was combined with protective serum.

GERMANY

BCG Vaccination.—F. Heisig (*Deutsche med. Wchnschr.* 84:1667, 1959) stated that the duration of the protection afforded by BCG vaccine is limited. It gradually decreases after three years. The vaccination achieves a general regression of active primary, postprimary, and generalized tuberculosis. There has been a striking reduction in the incidence of tuberculous meningitis among vaccinated persons. The ratio of vaccinated to nonvaccinated persons with tuberculosis was 1:10 in North-Rhine-Westphalia, 1:21 in the German Democratic Republic, 1:34 in Dresden, and 1:50 in Cottbus. Even previously tuberculin-negative nonvaccinated persons showed an incidence of tuberculosis seven times that of the vaccinated group. Other data similarly point to the effectiveness of BCG vaccination. A 51 to 66% reduction in incidence of tuberculosis within two years was observed among persons up to the age of 25 years in the district of Erfurt, and corresponding observations were made in other parts of the German Democratic Republic, Sweden, Denmark, and other countries where vaccination has been applied on a large scale.

Toxoplasmosis.—H. H. Kabelitz of Erlangen (*München. med. Wchnschr.* 101:1127, 1959) reported a series of 30 patients with toxoplasmosis. In the acute stage of the disease they were given 25 mg. of pyrimethamine three times a day for five days, then a sulfonamide for five days, and after this 25 mg. of pyrimethamine once daily for a prolonged period. The swelling of the lymph nodes subsided a few days after the beginning of treatment but recurred a few weeks later. This treatment, however, prevented the disease from becoming generalized. It is doubtful that complete cure was effected, since results of tests for antibodies, especially the Sabin-Feldman (S-F) test, were not negative even after apparent clinical improvement in the course of prolonged observations. The S-F and complement-fixation tests showed a decreasing titer, especially after treatment with the sulfonamide. After the completion of treatment the titers usually increased for a shorter or longer period and later fell permanently as the acute disease presumably enters a chronic stage.

Lipotropic Effect of Vitamin B_{12}.—Prof. F. Hartmann from Marburg, speaking at the 53rd conference of the Internal Medicine Society of Northwest Germany in June, stated that the deposition of neutral fat was identified as the cause of fatty changes in the liver. Choline can be formed in the body. Vitamin B_{12} exerts its lipotropic action by means of its role in the provision of active methyl groups. The experimental production of fatty livers in animals can be prevented by administration of vitamin B_{12}. This vitamin is necessary for the transformation of neutral fats into phosphatides. A decrease in the neutral fats and an increase in the phosphatide level was observed in 165 experimental animals treated with vitamin B_{12}. One is thus justified in attributing an absolute lipotropic effect to vitamin B_{12}. If the animals are given active methionine (methionine combined with ATP) plus vitamin B_{12} the effect is not completely additive. Exogenous unactivated methionine inhibits the effect of vitamin B_{12} given simultaneously, probably because by a sort of pharmacological law of mass action the exogenous unactivated methionine delays the formation of activated methionine in the body. The simultaneous administration of exogenous methionine and vitamin B_{12} is therefore illogical.

Tuberculous Superinfection.—E. Freerksen (*Deutsche med. Wchnschr.* 84:1617, 1959) stated that survival experiments in mice, guinea pigs, and rabbits showed that animals infected with minimal doses of Mycobacterium tuberculosis were able to survive superinfection with virulent organisms longer than those not so infected. The protective effect against superinfection was maximal two to six weeks after the initial infection, depending on the bacterial strain used. Within certain limits there was no definite correlation between protective effect and the vaccination dose, nor was the site of vaccination significant. Saprophytic mycobacteria produced no protection, but avirulent variants of pathogenic tubercle bacilli (BCG and H37Ra) provided good protection against superinfection. In mice a subcutaneous vaccination with virulent organisms provided definite protection against intravenous superinfection with the same virulent strain of tubercle bacillus, but this effect was not demonstrable in guinea pigs and rabbits, in which subcutaneous injection of virulent bacteria led to rapidly progressive tuberculosis. From this it was concluded that protection against superinfection with a virulent strain of tubercle bacillus is achieved only with a pathogenic form (Myco. tuberculosis, Myco. bovis, and Myco. microti).

Mycobacteria are designated as pathogenic if they cause the production of typical tuberculous foci in the infected host. This capacity is possessed by the pathogenic bacilli even when they have been killed. The pathogenicity factor probably resides within the phosphatide fraction of the tubercle bacillus. The development of tuberculosis as a disease requires not only pathogenicity of the micro-organism but also the capacity of intravital multiplication or virulence. Apparent virulence can be conferred on killed pathogenic micro-organisms by adjuvants which secure prolonged contact between the pathogenicity-factor and a given tissue. Virulence, however, is determined not only by properties of the micro-organism but also by the properties and conditions of the infected host. Thus, BCG is virulent for the golden hamster. Changes in these several factors are responsible for the activation of a previously inactive tuberculosis. In rare instances they may even lead to BCG tuberculosis in man.

Myco. avium, which is halfway between saprophytes and human or bovine tubercle bacilli, protects against tuberculous superinfection. The scotochromogenic, photochromogenic, and other atypical strains isolated from human lesions behave like Myco. avium. Protection against superinfection can be achieved, even with killed bacteria, if the dose of vaccine is large and the infecting dose small. Furthermore, the protective effect of killed bacteria can be augmented by adjuvants, but heterologous vaccines have failed to protect, except for a slight effect produced by poliomyelitis vaccine and a vaccine from an avirulent strain of Clostridium tetani. The protective effect is, if present at all, slightly increased by simultaneously administering chemotherapy. It has so far proved impossible to assign the protective effect of any one fraction or component of the tubercle bacillus or to establish a definite causal relationship between a sensitizing effect and protection against superinfection. It is thus necessary strictly to distinguish allergy from protection against superinfection. Tissue culture experiments and other studies indicate that protection against superinfection largely acts by improving the host's natural protective mechanisms. It is not simply an immunological phenomenon but part of the biological course of an infection.

Coronary Arteriosclerosis.—E. Hauch (*Ärztl. Praxis* 11:593, 1959) treated a series of 70 patients who had coronary arteriosclerosis with heparin in combination with beta-pyridyl-carbinol. Of these, 25 had had myocardial infarction. He injected a mixture of 5,000 to 10,000 units of heparin and 50 mg. of beta-pyridyl-carbinol two or three times a week, and to some he gave an additional 25 mg. of beta-pyridyl-carbinol three times a week by mouth. The vasodilator substance, beta-pyridyl-carbinol, has a strong and long-lasting effect on the coronary arteries and also improves the peripheral circulation. Control of the clotting time is not necessary with such small doses of heparin. Patients who have any condition which contraindicates heparin therapy should not be given this treatment. It is essential that the treatment be continued sufficiently long. The minimum period of treatment was two months and in some patients it was continued for three or four years. Even patients who react quickly should continue to receive treatment for a long period.

Of the 70 patients in the series, 61 were distinctly improved. The condition of myocardial insufficiency regressed continuously. Several of the patients were totally relieved of their symptoms and were able to dispense with the treatment with nitrites. In several the electroencephalographic changes became less marked, in some the electrocardiogram returned to normal. Patients who had been completely incapacitated by a previous infarct were able to return to work. In some patients a fall in the blood cholesterol level toward normal was observed after a few weeks, and in others with hypertension the blood pressure was found to fall gradually. Patients with coexistent disturbances of peripheral circulation observed relief of pain at rest, increase in the temperature of the extremities, and in the distances which could be walked. The treatment of coronary arteriosclerosis with heparin and beta-pyridyl-carbinol appeared to be a genuine advance.

Dermatitis Herpetiformis.—K. H. Schulz (*Hautarzt* 10:129, 1959) stated that in order to test the mechanism of the effect of sulfapyridine on dermatitis herpetiformis the 2-amino-pyridide of p-aminobenzoic acid was given to 16 patients in equal doses, with equally good results in each case. As a variation on the sulfapyridine formula the SO_2 group was replaced by a carbonyl group. Eleven patients were rendered symptom-free, three were improved, and two remained unaffected. Occasional gastric side-effects were observed. These results showed that the effectiveness of sulfapyridine cannot be ascribed to its antibacterial properties, that is, to the sulfonamide group.

Venesection in Portal Hypertension.—F. Reiman and co-workers (*München. med. Wchnschr.* 101:70, 1959) stated that treatment of hypertension by venesection has long been used, but hitherto it has hardly ever been tried in the treatment of portal hypertension. Since the development of diagnosis of this condition by percussion, however, splenic hemopuncture has been performed under local anesthesia on 10 patients with splenomegaly and portosplenic hypertension. A needle about 12 cm. long and 1.8 mm. in diameter was used. The first drops of blood were collected for morphologic and chemical analysis, the pressure was measured and 5,000 units of heparin were injected through the needle. This measure was found to be necessary in view of the high coagulability of the blood from the spleen.

The effluent blood was collected under sterile conditions in a transfusion bottle, the erythrocytes were transfused back again through the cubital vein, and the plasma was discarded. This retransfusion was done to maintain adequate oxygenation of the arterial blood in view of the sensitivity of the liver to hypoxia. Even though, with increasing experience, up to 500 cc. of blood could be withdrawn by this method, there was never any sign of anemia peripherally even before retransfusion. The operation was concluded by the intravenous administration of protamine sulfate, which produced an immediate cessation of bleeding on withdrawal of the needle. In one patient there was a transient splenic contraction, and two others showed a slight perisplenitis the day after the splenipuncture. No other side-effects were seen. In seven of the patients a fall in the splenic pressure to 150 mm. H_2O was observed. In three the pressure was unaffected. The spleen and liver showed a reduction in size and consistency for a few days. In one patient the reduction in size was permanent. If the method were ever to become more widely used the main indication would be for the treatment of patients with hemorrhage from ruptured esophageal varices and those in whom a reduction in portal hypertension is urgently desired.

UNITED KINGDOM

Influenza.—Careful watch on the course of influenza outbreaks is maintained at the World Influenza Center at Mill Hill under the direction of Dr. C. H. Andrewes. It is important to identify the virus responsible and to determine whether it is a lethal variant such as caused the epidemic of 1919. Moreover, if a new form of virus is responsible, vaccines to be effective must incorporate it because vaccines which confer protection against one strain of influenza virus may be ineffective against another. Three types of virus have been recognized: A and B, which are common, and C. It is their ability to undergo mutations which complicates the production of effective vaccines.

Much work has been done in this field since the Asian epidemic of 1957. New vaccines incorporating the older strains of virus and the new Asian strain are being produced. It is claimed that they will give up to 80% protection. The cost of a single injection is about one dollar. The experts believe that influenza viruses can lurk unknown for long periods in animal reservoirs. Even in a relatively mild epidemic effective vaccines are valuable. The Asian outbreak cost 28 million dollars in sickness benefit, probably twice as much in lost output, and a further large sum for medicines. Vaccine is available under the NHS. In an epidemic priority would be given to hospital staffs, family physicians, and others who would be at special risk to maintain essential health services.

Freedom to Grow.—An editorial (*Brit. M. J.*, Oct. 17, 1959) commented that the result of the general election should remind the medical profession that its fate is, to a large extent, bound up with party politics. For that reason medical members of Parliament should pay as much attention to British Medical Association policy on the National Health Service (NHS) as to the policies of their own and other political parties. If one looks at what the Conservative government has done in its recent period in office in the way of meeting the just claims of the nationalized medical profession, the picture is not encouraging. Before the election they criticized the Socialist handling of doctors' remuneration calling attention to the fact that Mr. Bevan had assured the medical profession that he accepted the substance of the Spens recommendations, but then did nothing to implement it, with the result that many physicians were forced by economic pressure to accumulate more patients than they could properly look after. On the other hand, the Conservative government itself deplored the Danckwerts award of 1952, which, so far as general practitioners were concerned, went far to implement the Spens recommendations. Their attitude was one of "This must never happen again." It is, however, reassuring to notice that they are interested enough in the Spens reports to give a concise summary of the effect of these on remuneration in the NHS.

In 1948 the doctors feared that as a result of the nationalization of their profession they would lose their status in the community and that this would in time discourage the best type of youth from taking up medicine as a career. The two Spens reports provided the two big sections of the profession in the NHS with a guarantee of a certain status within the community. If the new government puts the two Spens reports into the discard, the profession must make sure that it will secure a new charter that will safeguard its future status and not be tempted by any immediate monetary advantage to overlook the importance of this factor.

In 1949 the Conservative party stressed the comprehensive nature of the NHS and the fact that any part of it should be available to any member of the public. They accepted the logical position that private patients should therefore be able to obtain, free of charge, drugs prescribed by their physician on a parity with people in the state scheme. Ten years later the Campaign Guide of 1959 had to admit that private patients are not yet able to do this, though there is nothing contrary to Conservative principles in the supply of drugs in this way to private patients.

The next five years are bound to see modifications in the NHS. Its virtues and defects after 10 years' experience are becoming more clearly defined. Much in it is good, and much in it is bad, and the job of the profession in cooperation with the government is to see that the bad is removed and that the good is made better. If the Royal Commission succeeds in finding an acceptable formula for the settling of future remuneration of doctors in the NHS, then the way will be clearer for cooperation between profession and government in bringing into being such valuable measures as the mental health bill which was introduced last January on the basis of recommendations made by the Royal Commission set up in 1954. The NHS needs freedom to grow.

CORRESPONDENCE

PATIENTS REFERRED FOR CHECK-UP

To the Editor:—Dr. Ralph W. Ballin's letter in The Journal, Oct. 24, page 1143, contains generalizations that should be clarified. There are relatively few manifestations of generalized systemic disease that appear in the eye, and most of these are known by the patient and his family physician well before the patient is ever seen by an ophthalmologist. It is the ophthalmologist's duty to notify the patient's physician of his findings, but it is not his responsibility to complete the medical examination or to prescribe the medicaments required, if any.

Arteriosclerotic and degenerative conditions are slowly progressive, and there is no evidence that any local or systemic medication will delay their progression in the eye. The only symptom the patient has is slow loss of vision. This can be temporarily benefited by increasing the strength of the glasses, producing the magnification necessary to read. I have seen hundreds of patients with arteriosclerotic and degenerative eye disease, who have been treated for years by physicians who had them spend all of their small retirement income in futile treatment, when telling them the truth about their disease would have saved a great deal of money during the advanced years when every dollar is vital. Any physician who accepts an optometrist's referral of a patient for treatment of an eye condition should immediately refer the patient to an ophthalmologist. An optometrist's main function is to prescribe glasses. He is in no way trained to diagnose or treat eye diseases. The American Optometrist Society has decreed that, when eye disease is suspected, the patient should be referred to his family physician and not to an ophthalmologist. This results in confusion, because the physician does not have a specialist's knowledge of the eye. Only future education will remedy this condition.

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CHILDHOOD SCHIZOPHRENIA

To the Editor:—I think it would be wise to exercise caution regarding the conclusions of Koegler and Colbert in their article on childhood schizophrenia in The Journal, Oct. 24, page 1045. Many other experts do not accept a primarily physiological basis for childhood schizophrenia, and, to date, there are no incontrovertible biochemical or physiological findings in adult or childhood schizophrenia.

One of the most recent biochemical studies (Mann and LaBrosse: *A. M. A. Arch. Gen. Psychiat.* 1:547 [Nov.] 1959) reported no difference in findings between childhood and adult schizophrenics and controls. Kanner, who originated the term "childhood autism," found no evidence for genetic factors in these children, and Szurek and his collaborators, after 10 years of intensive research, concluded that childhood schizophrenia has a psychological etiology.

References to the reticular formation or the limbic system have become *de rigueur* in physiologically oriented articles on behavior. Such speculations do not do justice to the complex and varied results obtained in animal studies.

Childhood schizophrenia is probably a combination of disorders, and general statements about it can therefore be misleading. There may have been good reason for Bleuler's titling his famous book *The Group of Schizophrenias.* How far have we come in the past 50 years? The family physician should keep an open mind on this most recondite problem.

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AUGMENTATION MASTOPLASTY

To the Editor:—I have received several inquiries regarding the letter to the editor in The Journal, May 2, page 140, entitled "Augmentation Mastoplasty." I am afraid it gives a distorted picture of the current state of affairs. The use of various synthetic sponges to increase breast size has become increasingly successful within the last two or three years. These are the materials that have been used for many years in reconstructing heart valves and other structures in cardiovascular surgery. Some of the newer materials do not show the disadvantage of hardness that was seen with the earlier materials. In any event, the success of many of these operations has been outstanding with regard to profound and apparently beneficial psychological changes. There is some danger of infection in any surgical operation, and with the use of any foreign implant this rate of infection probably increases. It has not, however, proved to be a dangerous or serious drawback to the use of this procedure, in my experience.

The psychological changes effected by such procedures would constitute a much more valid reason for careful decision with regard to this type of operation than any drawback from actual surgical complications. My own experience with this operation over a 10-year period has been most encouraging. In only one instance in that period have I had to remove an implant that I inserted.

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MISCELLANY

REQUIREMENTS FOR ACCEPTING HOSPITALS FOR LISTING BY THE AMERICAN HOSPITAL ASSOCIATION

The primary aim of the program of accepting hospitals for listing is to provide a census of hospitals. Listing is not intended to be a measure of quality of care.

Any institution which can be classified as a hospital, according to the requirements, may be listed if it so desires. Membership in the American Hospital Association is not a prerequisite.

1. The hospital shall have at least six beds for the care of patients who are nonrelated, who are sick, and who stay on the average in excess of 24 hours per admission.
2. The hospital shall be licensed in those states and provinces having licensing laws.
3. Only doctors of medicine or doctors of osteopathy shall practice in hospitals listed by the American Hospital Association. (This requirement is not intended to eliminate dental and similar services from the hospital. Patients admitted for such services, however, must have an admission history and a physical examination done by a physician on the medical staff of the hospital, and a physician on the medical staff of the hospital shall be responsible for the patient's medical care throughout his stay.)
4. Duly authorized bylaws for the medical staff and staff of physicians shall be adopted by the hospital.
5. The hospital shall submit evidence of regular care of the patient by the attending physician and of general supervision of the clinical work by doctors of medicine.
6. Records of clinical work shall be maintained by the hospital on all patients and shall be available for reference.
7. Registered nurse supervision and such other nursing service as is necessary to provide patient care around the clock shall be available at the hospital.
8. The hospital shall offer services more intensive than those required merely for room, board, personal services, and general nursing care.
9. Minimal surgical or obstetrical facilities (including operating or delivery room), or relatively complete diagnostic facilities and treatment facilities for medical patients, shall be available at the hospital.
10. Diagnostic x-ray services shall be regularly and conveniently available.
11. Clinical laboratory services shall be regularly and conveniently available.

The American Hospital Association may, at the sole discretion of its Board of Trustees, grant, deny, or withdraw the listing of any hospital.

As amended and approved by the Board of Trustees, Aug. 26, 1959.

MEDICAL FILM REVIEWS

The Human Body: Reproductive System: 16 mm., color, sound, showing time 13 minutes. Educational collaborators: John S. Gray, M.D., and Albert Wolfson, Ph.D., Northwestern University. Produced in 1959 by and procurable on purchase from Coronet Instructional Films, Coronet Building, Chicago 1.

This film describes the male and female reproductive organs and the functions of each, showing the major stages of human embryonic development. Actual views of live human sperm and ova uniting to form the zygote are shown by photomicrography. Animation is used to show the similarities and differences in the organs of both sexes and serves to clarify their functions. The film is authentic, carefully prepared, and should be useful in the biological study of the various systems of the body. It might well be included in a program of family life education planned to include the anatomic and physiological aspects of reproduction. The moral and ethical considerations should be included in discussion after the showing of the film. It is recommended for use in situations where the community has sanctioned the inclusion of sex education in the schools.

NEW FILM ADDED TO A. M. A. MOTION PICTURE LIBRARY

Management of Breast Feeding: 16 mm., black and white, sound, showing time 14 minutes. Prepared by Gordon D. Jensen, M.D., Seattle. Produced by and procurable on rental ($2) or purchase ($45) from Film Center, University of Washington, Seattle 5.

This is a good film on the subject of breast feeding. It begins with an explanation of breast care to the expectant mother. The woman's questions are answered simply. The nurse in the hospital also plays a part in helping carry out instructions and giving the patient confidence. Engorgement and the anatomy of the breast and the nursing procedure are shown in diagram. Manual expression of the breast is also shown. The photography and narration are good and the sequences are clear and easy to follow. This film is highly recommended for medical students, house staff, and all those involved with the care of the nursing infant. It would also be a good film to show to mothers before term.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Long-Term Survival Following Onset of Congestive Failure: Case Report. P. L. Rettew. Pennsylvania M. J. 62:1326-1329 (Sept.) 1959 [Harrisburg].

The author presents the case of a 65-year-old man who in May, 1948, had to discontinue working because of weakness, edema, and dyspnea. In August, 1948, he resumed work, but edema gradually returned despite 3 injections of a mercurial diuretic, appropriate amounts of ammonium chloride, and digitalis. In December, 1948, physical examination revealed orthopnea. The skin was cold, dry, and scaly. Coarse rales were detected in the posterior lung bases, and the heart was greatly enlarged. Atrial fibrillation was present. A mitral systolic murmur was heard. Marked pitting edema was present, extending to the midscapular region; ascites was noted. A roentgen-ray film of the chest in December showed enlargement of all cardiac chambers. Shallow, diffuse pulsations were seen on fluoroscopy. A pleural reaction and exaggerated vascular markings were noted. The aorta was calcified. An intravenous urogram showed calcification of the pelvic blood vessels and only faint visualization of the urinary structures. A diagnosis of arteriosclerotic heart disease complicated by congestive failure was made. Treatment consisted of the administration of mercurials, ammonium chloride, and digitalis leaf. A diet containing 200 mg. of sodium was prescribed. Complete bed rest was carried out.

The patient lived 9½ years with hypertensive heart disease after the first episode of severe failure. For the last 8½ years of his life, no cardiac drugs were given. A low-sodium diet appeared to be adequate for complete control of the heart failure. While failure occurred in the last 24 hours of life, this was thought to be a terminal phenomenon. It is generally accepted that, once digitalized for heart failure, a patient must continue with a maintenance dose indefinitely. The experience of some physicians would suggest, however, that at times digitalis can be omitted with safety. This patient is presented as an example of a successful maintenance of compensation without digitalis. The author cites a report by Rogen, according to which, of 20 patients treated for acute failure by digitalization, none could omit maintenance doses longer than 8 weeks. Most of these cases were of rheumatic etiology; only 3 were arteriosclerotic or hypertensive. In the patient presented, there were no findings to suggest infarction as the cause of the initial episode of profound failure. No gross infarcts were evident at autopsy. Individual appraisal of each case is necessary, because therapy should depend upon an understanding of the mechanism of failure in each patient.

Assessment of Mitral Valve Disease by Left Heart Catheterization. E. W. Hancock. Brit. Heart J. 21:389-400 (July) 1959 [London].

Assessment of the relative importance of mitral stenosis and regurgitation, when present in combination, has remained a difficult problem. This report summarizes experience with left heart catheterization in 75 patients with mitral valve disease, with particular reference to the assessment of combined stenosis and regurgitation. Left atrial puncture was carried out by the right posterior transthoracic route, as described by Biork and associates in 1953. The procedure caused no deaths or cardiac tamponade. Hemoptysis and pneumothorax occurred in 16 of the patients, but these complications became less frequent with experience. Delayed arterial embolism occurred twice. The left atrium was successfully punctured in every case, and the left ventricle successfully catheterized in all but 3 of the 75 patients. The author gained the impression that in pure mitral stenosis the severity of the lesion may be accurately assessed if the pressure gradient across the valve and the cardiac output are determined together. Clinical signs of mitral stenosis may be present in the absence of a significant pressure gradient.

Five patients of this series had severe mitral stenosis in the absence of a diastolic murmur. In pure mitral regurgitation there is no significant pressure gradient across the valve in diastole. These patients cannot always be distinguished from those with predominant mitral stenosis by the clinical signs. Diastolic murmurs and pulmonary hypertension are commonly present. In combinations of mitral stenosis and regurgitation, large diastolic pressure gradients are commonly present,

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The place of publication of the periodical appears in brackets preceding each abstract.

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even when regurgitation is the dominant lesion. Exact assessment of the valve size in this group is limited by inability to measure regurgitant flow. Estimation of a minimal valve area is of considerable value, and further information is gained from the left atrial pulse form and from dye dilution curves. Left heart catheterization has proved a practical and useful diagnostic procedure in patients with mitral valve disease in whom clinical assessment is difficult.

Postmyocardial Infarction Syndrome. N. J. Weiser, M. Kantor and H. K. Russell. Circulation 20:371-380 (Sept.) 1959 [New York].

A syndrome likely to develop after myocardial infarction was first described by Dressler in 1956; until January, 1959, this investigator had observed 53 cases, and had estimated its incidence in patients with acute myocardial infarction at approximately 3%. The syndrome is characterized by prolonged or recurrent fever, chest pain, and clinical and laboratory evidence of pericarditis, pleurisy, and pneumonitis. These abnormalities may occur alone or in combination, and all show tendency to recurrence. The authors present the histories of 4 patients with this syndrome, all men, ranging in age from 43 to 64 years. The symptoms of the postmyocardial infarction occurred as early as 5 days and as late as 2 years after the infarction. They included prolonged or recurrent pericarditis in 2 cases and hemorrhagic pneumonia in 2 cases. None of the 4 patients had pleural effusion. Three of the 4 patients were febrile beyond the period of acute myocardial infarction, and one had chest pain which could not be accounted for by infarction. Failure to recognize this syndrome resulted in misdiagnosis in 2 of the 4 patients. In the third patient prolonged pericarditis with effusion was diagnosed, and the fourth suffered the major manifestations of his illness at another hospital.

In 2 of the 4 patients hemoptysis and pulmonary infiltrations developed within a few hours after the substernal pain that signaled the onset of the infarction. One of these patients showed these symptoms on at least 2 and perhaps 3 occasions. In both patients the authors made a diagnosis of almost simultaneous pulmonary and myocardial infarction, attributing the pulmonary infarction to the previous history of arteriosclerotic heart disease and the myocardial infarction to the fall in blood pressure consequent to the pulmonary infarction. The explanation is labored enough, although supported by previous clinical experience; however, it was made even less tenable in one patient by the clinical and radiologic evidence of progressive hemorrhagic consolidation of both lungs in the face of well-controlled anticoagulant therapy. The unresponsiveness to anticoagulants was sufficient to call the attention of the authors to the true state of affairs in this patient, and they feel that in the other patient the coincidence of pulmonary and myocardial infarction might reasonably have been accepted once, but not twice.

Since the illness is usually self-limited, symptomatic therapy with salicylates, analgesics, or narcotics suffices for the majority of cases. Corticosteroids have been found to be almost specific, causing fever and chest pain to disappear within 24 hours. However, rebounds have been observed frequently after withdrawal. Therefore, these drugs have been reserved for patients with excruciating pain or with an unduly prolonged illness. The cause of this syndrome remains unknown. Attempts to implicate an infectious process, bacterial or viral, have been unsuccessful. Antibiotics have had no effect on the clinical course. Anticoagulant drugs were suspected, but cases have been found in which no such treatment was administered. The clinical features of the postmyocardial infarction syndromes resemble those also seen in the postcommissurotomy syndrome. It has been suggested that the latter actually represents a hypersensitivity reaction to antigens produced by the traumatized heart, and the same type of mechanism may underlie the postmyocardial infarction syndrome.

Left Atrial Pressure Pulses in the Presence of Myxoma. R. G. Fish, T. Takaro and T. Crymes. Circulation 20:413-418 (Sept.) 1959 [New York].

Left atrial myxoma is usually discovered at the time of atriotomy for a planned mitral commissurotomy. With this discovery, the procedure must be abandoned, and preparations must be made for a second thoracotomy and cardiopulmonary bypass. As far as the authors know, there has been no report on findings obtained on left heart catheterization in the presence of a left atrial myxoma. They describe studies on a 51-year-old man, in whom a mistaken diagnosis of pure mitral stenosis had been made. His clinical picture was devoid of any feature that might arouse suspicion of an atrial myxoma, but exploration revealed an entirely normal mitral valve and a large atrial myxoma on the left side. Transbronchial left heart catheterization was performed on this patient, and pressure recordings were made. Mean left atrial pressures were obtained electronically. In addition to an elevated mean left atrial pressure and ventricular filling gradient, the pressure pulses obtained were characterized by a brief initial period of apparently unobstructed left atrial outflow and by differences in contour between high and low left atrial recordings. These dissimilarities are thought to reflect the different pressure relationships that occur above and below the tumor.

The authors do not wish to imply that left heart catheterization or selective left atrial angiocardiography is the most desirable method of study in those cases in which the existence of a myxoma may be suspected. The danger of dislodging emboli from a friable myxoma by needle insertion or high-velocity dye injection makes these procedures unsafe. Venous angiocardiography is the diagnostic procedure of choice in this situation.

Effects of Infusion of Acetylcholine on Pulmonary Vascular Resistance in Patients with Pulmonary Hypertension and Congenital Heart Disease. J. T. Shepherd, H. J. Semler, H. F. Helmholz Jr. and E. H. Wood. Circulation 20:381-390 (Sept.) 1959 [New York].

Survival after surgical correction of congenital cardiovascular defect is unlikely if pulmonary hypertension cannot be decreased significantly. Acetylcholine causes local vasodilatation when injected intra-arterially into systemic vessels. Rapid inactivation of this substance in the circulating blood makes possible its injection into the pulmonary artery in sufficient concentration to affect the pulmonary vessels without altering the hemodynamics of the systemic circulation. The authors administered acetylcholine by constant-rate infusion into the pulmonary arteries of 11 patients with pulmonary hypertension associated with atrial or ventricular septal defects. The oxygen consumption, oxygen saturation in the pulmonary artery and systemic arterial blood, and the pulmonary artery pressure were recorded continuously before, during, and after the infusion. These data were used to determine changes in total pulmonary resistance during infusion of acetylcholine. All 6 patients with atrial septal defects showed some decrease in resistance when receiving acetylcholine. If the pulmonary resistance when the patient was breathing air was taken as 100%, the decrease was 23% (range, 15 to 51) with infusion of acetylcholine alone, 29% (range, 9 to 33) on breathing oxygen, and 43% (range, 27 to 60) on breathing oxygen and receiving acetylcholine.

Of the 4 patients with only ventricular septal defects, one did not respond to either oxygen or acetylcholine. For the remainder, the average percentage decrease in resistance with acetylcholine while breathing air was 31% (range, 10 to 69); while breathing oxygen, 33% (range, 25 to 66); and while breathing oxygen and receiving acetylcholine, 57% (range, 35 to 74). One patient with both an atrial and a ventricular septal defect showed no response. As there was no evidence of a decrease in left atrial pressure with acetylcholine, these changes in total pulmonary resistance, demonstrated by the method employed, presumably represent an actual reduction in pulmonary vascular resistance. It is concluded that active constriction of pulmonary vessels can be an important factor in maintaining the high resistance to pulmonary blood flow found in some patients with congenital heart disease.

Note on a Monstrous Finger. W. B. Bean and P. K. Peterson. A. M. A. Arch. Int. Med. 104:433-438 (Sept.) 1959 [Chicago].

The authors report a case of local gigantism in a 53-year-old man with a monstrous finger, who was admitted to the University Hospitals of the State University of Iowa College of Medicine in Iowa City. At the patient's birth, his mother noticed that the middle finger of the left hand was much bigger than the middle finger of the right hand. The 4th finger of the left hand was slightly enlarged. The growth rate of these fingers approximated that of the other fingers, so that the discrepancy in size persisted throughout the period of growth. There had been no similar deformity in any members of the patient's family. There was no history of acromegaly. Roentgenograms of the patient's left hand revealed the bones and joints to appear normal, as were the soft tissues, with the exception of the disproportion in size. This was interpreted as primary localized gigantism rather than as secondary gigantism. There were no indications of neurofibromatosis, angiomatosis, or any other vascular or lymphatic anomaly to explain this prodigy. Thus, there is no present explanation why, in this particular patient, a digit, which was already abnormally large at birth, continued throughout growth to maintain its relative disproportion and to present a grotesque, but not a crippling, deformity.

Clinical Primary Hyperparathyroidism. C. C. Johnson and W. D. Forney. A. M. A. Arch. Int. Med. 104:390-395 (Sept.) 1959 [Chicago].

The authors report on 8 patients with primary hyperparathyroidism, resulting from a single parathyroid adenoma in 7 and from multiple adenomas in 1. The cases of these patients were identified in clinical practice in Idaho in the past 5 years. None of the 8 patients had progressed to the stage in which roentgenographic bone findings were present. The presenting symptoms in 7 patients were those referable to renal calculi; the 8th patient had not only renal calculi but also renal calcinosis. In all but one of the 8 patients, the renal calculi were present bilaterally at some time. There had been 8 operations for renal calculi, and of these 8, 2 were nephrectomies because of severe renal damage. Two patients had re-formed renal calculi removed a second time. Other less common symptoms, which were frequently observed in these patients, were constipation, nervousness, polyuria, lethargy, weight loss, and muscle pain. Three patients had a diastolic blood pressure above 90 mm. Hg.

The diagnosis of primary hyperparathyroidism depends first on a suspicion of the existence of such a condition. All patients with calculi should have an investigation for possible parathyroid hyperfunction. Hypercalcemia and hypophosphatemia are the most important diagnostic clues to hyperparathyroidism. The serum calcium level was above 11 mg. per 100 cc., and the serum phosphorus level below 3 mg. per 100 cc., in all except 3 patients. None of these patients were subjected to stress tests. In all patients the diagnosis was verified at surgical intervention. The chief significance of hyperparathyroidism is the irreversible damage produced to various tissues of the body if the condition is permitted to continue. There is no problem in recognizing hyperparathyroidism, once symptoms characteristic of generalized osteitis fibrosa have developed in the patient. With the present knowledge of the disease, very few patients should ever reach this late stage. Once a diagnosis of hyperparathyroidism is made, a surgeon is committed to find and remove all the excess hyperfunctioning tissue. Once the excess parathyroid stimulus has been removed, the calcium is rapidly deposited in bones again, and the deposition may be at such a rate that the serum calcium is lowered to abnormally low levels, with the result that tetany occurs. It may be necessary to administer to the patient intravenously calcium or even dihydrotachysterol (Hytakerol) for a few days or weeks after surgical intervention.

Chronic Adrenocortical Dysfunction, Including Aldosterone Deficiency: Studies of Steroid and Electrolyte Metabolism. G. D. Molnar, V. R. Mattox, H. L. Mason and M. H. Power. J. Clin. Endocrinol. 19:1023-1036 (Sept.) 1959 [Springfield, Ill.].

The authors carried out metabolic studies on a 44-year-old man in whom acute adrenal insufficiency, with vascular collapse and characteristic changes in electrolytes after a minor surgical procedure, called attention to an unusual form of adrenocortical dysfunction of at least 20 years' duration. Excretion of aldosterone was less than 0.5 mcg. per 24 hours and was not increased by restriction of sodium or administration of corticotropin or corticosterone. Loss of sodium and retention of potassium occurred with hyponatremia and hyperpotassemia during a period when the daily sodium intake was less than 200 mEq. Normal values for electrolytes were restored by the administration of aldosterone or fludrocortisone but not by the administration of corticotropin or cortisone. Values of plasma and urinary corticosteroids were normal but were not increased by the infusion of corticotropin. Hydrocortisone and cortisone were identified in the urine. Results of glucose tolerance tests were normal. Diuresis after ingestion of water was impaired. Urinary excretion of 17-ketosteroids was in the high normal range, and that of pregnanetriol and estrogens was moderately increased; the values for these constituents were not increased by the administration of corticotropin but were decreased by that of cortisone or corticosterone.

These findings showed that the abnormalities in electrolyte metabolism in this patient resulted from a deficiency of aldosterone. The reported data do not support the possibility that he had primary renal disease. The patient had had attacks typical of adrenal insufficiency 20 and 14 years previously, with nausea, vomiting, and symptoms of postural hypotension. Symptoms and findings had not changed appreciably in the interim. The patient had a craving for salt, as well as mild polyuria and polydipsia, for as long as he could remember. One can only conjecture about the mechanism by which the abnormalities in this patient were acquired. It is not known whether his adrenal cortices were, in fact, hyperplastic, as is suggested by similarities to the syndrome of virilizing adrenal hyperplasia with salt-losing features. On the other hand, it is possible that he was born with an enzymatic defect, affecting the elaboration of adrenal steroids, which might not have become quantitatively significant until adult life. Among the enzymatic disturbances, a deficiency of 21-hydroxylase might be the major and most reasonably postulated one.

Familial Occurrence of Gastric Ulcer: Casuistic Report. A. Nordøy. Tidsskr. norske laegefor. 79:951-953 (Aug. 15) 1959 (In Norwegian) [Oslo].

In a larger material the frequency of peptic ulcer is found to be about 2 to 2½ times as high among relatives of patients with the disease as it is in the population in general. Members of the families of patients with gastric ulcer have a tendency to gastric ulcer, and relatives of patients with duodenal ulcer have a tendency to duodenal ulcer. Seen from a genetic standpoint, gastric ulcer and duodenal ulcer are to be considered independently of each other. In the family reported on, gastric ulcer was established in the father and 4 sons. These persons have, in the main, lived in similar environments and under similar nutritional conditions. It seems clear that hereditary circumstances must be considered with reference to the complicated genesis for ulcer disease. It is difficult to say whether the genetic factor follows the blood group. Evidence suggests that the genes concerned are related to the blood types in the ABO system.

SURGERY

Indications and Contraindications for Surgery in Ventricular Septal Defect. C. A. Neill and H. B. Taussig. J. Pediat. 55:374-381 (Sept.) 1959 [St. Louis].

Now that closure of ventricular septal defects is widely practiced, the pediatrician should know not only the possible benefits of surgery but also the possible risks. The authors discuss only those patients in whom the ventricular septal defect occurs as an isolated malformation or in association with slight overriding of the aorta. Three main groups of patients are considered; namely, those with small ventricular septal defects and small shunts, those with moderate-sized or large defects and large left-to-right shunts, and those with cyanosis and a reversed or right-to-left shunt, that is, the so-called Eisenmenger complex.

The authors are of the opinion that patients with small ventricular septal defects and small left-to-right shunts, the so-called maladie de Roger group, should not be operated on at the present time, because there is no risk of the development of pulmonary hypertension and because the risks of surgery outweigh any possible benefits. Patients with mild or moderate pulmonary hypertension show a steady level of pulmonary artery pressure during the childhood years, and in many instances the pulmonary artery pressure falls as the years pass. This is in contrast to the commonly held idea that pulmonary hypertension is steadily progressive throughout childhood and makes surgery a matter of urgency in all children with ventricular septal defect. These children can be greatly benefited, and surgery is indicated for them if the operative risk can be kept at minimal levels.

Children with large left-to-right shunts and severe pulmonary hypertension are the major problem at the present time, both in management during infancy and in selection of the best time for operation. Although operation in infancy remains dangerous, it may in rare instances be justified. Certainly operation in early childhood is to be considered in those children with severe right ventricular hypertrophy and a sufficiently large defect in order to insure that blood is being ejected into the lungs at systemic levels of pressure or under a "common ejectile force." Patients with shunt reversal, cyanosis, fixed pulmonary resistance, and a predominant right-to-left, rather than a left-to-right, shunt are classified as having the Eisenmenger complex and are not candidates for surgery until understanding of the postoperative management of pulmonary hypertension increases. The selection of patients for open-heart surgery is now firmly based on physiological studies and on increased [illegible] importance of the pulmonary vascular bed.

Results of Treatment of Papillary Carcinoma of the Thyroid. G. Crile Jr., J. M. McNamara and J. B. Hazard. Surg. Gynec. & Obst. 109:315-320 (Sept.) 1959 [Chicago].

The authors report on 107 patients with papillary carcinoma of the thyroid for which they were operated on. Nineteen patients were excluded; 12 of these had been operated on less than 5 years ago, and 7 died in less than 5 years of causes other than thyroid cancer. Of the remaining 88 patients, 8 died; 5 died of carcinoma of the thyroid within less than 5 years after the operation, 1 died of carcinoma of the thyroid more than 5 years after the operation, and 2 died of other causes than carcinoma more than 5 years after the operation. Thus, 83 of the 88 patients survived 5 years after the operation, i. e., a 5-year survival rate of 94%, and that despite the fact that 75% of the cancers had metastasized at the time of operation. Eighty patients (90.9%) are living 5 to 20 years after the operation, and 76 of these (86.4% of the 88 patients) do not have any evidence of carcinoma of the thyroid.

After operations that remove all grossly involved tissues but conserve uninvolved muscles and nerves, local recurrences have not been a serious problem. There is no case in this series in which there has been a recurrence in the sternomastoid muscle. None of the 74 patients in this group who were given primary treatment by the authors has died with a local recurrence of a thyroid cancer or now has evidence of persistent cancer in the neck or mediastinum. All these patients have been followed for an average of 8½ years. The operation required in any given case depends on the extent of the disease, but always should include wide resection of the primary tumor. If the regional lymph nodes are explored and there is no gross evidence of metastasis, there is no necessity for prophylactic dissection of the neck. In only 1 of 25 such patients did cervical metastasis develop after operation, and in this patient it was easily controlled by excision of a single involved node. If the cancer is localized to a single lobe of the thyroid, complete removal of that lobe, sometimes with the isthmus and a part of the contralateral lobe, is all that is required. In none of 75 such patients has cancer appeared in the contralateral lobe. The high survival rate observed in this series is probably due to (1) removal of all grossly recognizable tumor in the vital central cervical and superior mediastinal areas, (2) routine daily feeding of 2 or preferably 3 grains (120 or 200 mg.) of desiccated thyroid after all operations for papillary cancer, and (3) exclusion from the classification of papillary carcinoma of the cases in which there were elements of anaplastic cancer.

The Role of Radical Surgery in the Treatment of Abscess of the Brain. H. T. Ballantine Jr. and C. N. Shealy. Surg. Gynec. & Obst. 109:370-374 (Sept.) 1959 [Chicago].

The authors report on 44 patients with abscess of the brain, who were admitted to the Massachusetts General Hospital, Boston, and on 40 of whom operations were performed. The primary procedure, which was intended by the surgeon as definitive treatment of the abscess, consisted of aspiration (simple tapping with a needle) in 16 patients, evacuation (open surgical drainage of the abscess without removal of the capsule) in 10, and primary excision in 14. Aspiration failed to produce a cure in 10 of the 16 patients. Two of the 10 patients were moribund before the operation and died; 5 of the remaining 8 survived after subsequent evacuation or excision, but the other 3 died because irreversible damage had occurred before more adequate drainage was performed. Evacuation failed to produce a cure in 6 of the 10 patients; one patient died without further therapy, and 4 of the other 5 survived after subsequent excision. Four of the 14 patients treated by primary excision died. Two of these were in a dying state before the operation, one patient failed to recover from a postoperative temporal lobe pressure cone, and the cause of death of the 4th patient could not be determined.

A comparison of these methods of therapy in the poor-risk (comatose) patients revealed that aspiration was successful in only 1 of 7 patients, evacuation was successful in 1 of 4, and excision was successful in 5 of 7. Late postoperative results in the patients who survived the operation revealed that 3 of 6 patients treated by aspiration alone were left with considerable neurological residuals (hemiparesis or aphasia). Evacuation, when successful, resulted in complete recovery. In the excision group, 8 of 9 patients with primary excision had no postoperative deficit, and the condition of one was improved over his preoperative status. On the other hand, of the 9 patients with an excision secondary to aspiration or evacuation, 8, although improved, still had residual deficits, and 1 patient was essentially unimproved neurologically.

The results obtained in these patients suggest that excision offers the best chance for cure of a brain abscess. Excision of brain abscess results in a lower morbidity than aspiration. Neurological residual deficits occur less often in patients with primary excision than with secondary excision. Although aspiration will cure some patients, many will require other more radical surgical intervention, and some will die before other procedures can be carried out. There is no evidence that surgical intervention results in spread of sepsis from a brain abscess if proper antibiotic treatment is used. Once the diagnosis of brain abscess is made, the condition should be considered a surgical emergency.

The Solitary Circumscribed Pulmonary Lesion Due to Bronchogenic Carcinoma: a Three-Year Follow-up Study of 94 Surgically Treated Patients. J. W. Vance, C. A. Good, C. H. Hodgson and others. Dis. Chest 36:231-237 (Sept.) 1959 [Chicago].

The data on 94 patients with bronchogenic carcinoma, who were treated surgically at the Mayo Clinic during 1944-1954, are analyzed. This series was selected according to 3 criteria: 1. Roentgenologic evidence of a solitary pulmonary lesion must have existed at the time the patient was first seen. The lesion had to be in the substance of the lung, to have a more or less well-defined border, and to be more or less round. 2. The lesion could not be associated with peripheral obstructive changes, central cavitation, or pleural effusion. 3. The diagnosis of bronchogenic carcinoma must have been made on the basis of pathological examination of the excised lesion. There were 76 men and 18 women in this series; with the exception of 2 patients, all were over 40 years of age. Eighty-five patients (90%) were considered to have operable disease at the time of examination. The 9 patients without possibility of resection underwent exploratory thoracotomy. The following types of operation were performed: pneumonectomy, 44 (2 palliative); bilobectomy, 8 (1 palliative); and lobectomy, 33.

Five of the 82 patients who underwent resection with a view to cure died in the hospital. Seven of the 9 patients who had only exploratory thoracotomy died within the first year after operation; the 8th patient died during the second year, and the 9th during the third year. The 3 patients who received palliative surgical treatment died during the first year after operation. Of the patients available for a 3-year follow-up study, 76 were traced. Thirty-four of them (44.7%) lived 3 or more years after the resection, so that, taking the series as a whole, the 3-year survival rate was 36.6%. Compared with a previous series reported, also from the Mayo Clinic, there was no essential difference in the 3-year survival rate for resectable bronchogenic carcinoma, whether or not it presented on the thoracic roentgenogram as a solitary circumscribed pulmonary lesion. The similarity of results supports the proposition that distant spread of solitary circumscribed lesions of bronchogenic carcinoma occurs more by vascular pathways than by the lymphatic system. Although early diagnosis and early surgical resection offer the greatest hope for improvement of survival rates, the most favorable lesions have been associated with a survival rate of about 50%.

Tuberculosis of the Lungs, Pleura and Mediastinum Diagnosed by Exploratory Thoracotomy, with Special Regard to Value of Brief Preoperative Antituberculosis Chemotherapy. H. E. Jensen. Nord. med. 62:1227-1230 (Aug. 13) 1959 (In Danish) [Stockholm].

In the thoracosurgical department of Øresund Hospital, Copenhagen, thoracotomy is performed on every patient in the cancer-suspect age if within 2, or at the most 3, weeks it has not been possible to make certain diagnosis or to exclude cancer. In 60 patients admitted during the 9 years up to the end of 1957, certain preoperative diagnosis could not be made. Most of the patients were in the cancer-suspect age. Before operation, 23 patients received antituberculosis chemotherapy for 2 or 3 weeks, 32 had no preliminary treatment, and in 5 the preliminary treatment was concluded than 2 months earlier or was brief. After operation, all the patients were treated at once with streptomycin and as quickly as possible with aminosalicylic acid; since the end of 1953 they also received isoniazid. Three patients died postoperatively. The 57 surviving patients were followed up for 6 months in 2 cases and for 1 to 8 years in 55 cases. Spread of tuberculosis was found in 6 cases, with development of tuberculous cavities in 4 of these; in 1 case there was miliary tuberculosis; and in 1 instance pulmonary cancer had developed, with dissemination of the tuberculosis, and the patient had died. Long-continued medicamental treatment of tuberculosis before resection is aimed exclusively at preventing tuberculous spread or activation of small, not recognizable foci.

Extirpation of the Spleen. K. Ohma. Tidsskr. norske laegefor. 79:953-955 (Aug. 15) 1959 (In Norwegian) [Oslo].

In surgical division B of the Rikshospital, Oslo, during the 10-year period ending May, 1959, 84 splenectomies were performed in 37 men, whose average age was 37 years, and in 47 women, whose average age was 42 years. Six patients died postoperatively, giving a mortality of 7.1%. If purely hematological indications are considered, without reference to leukemias and sarcomas, 73 patients were operated on, with a mortality of 4.1%. The normal weight of the spleen is 150 to 200 Gm. In the 23 cases of hemolytic anemia the average weight was 567 Gm.; in the 6 cases of aplastic anemia, 233 Gm.; in the 2 cases of granulocytopenia, 495 Gm.; in the 3 cases of Felty's syndrome, 973 Gm.; and in the 2 cases of anemia myelofibrosa, 1,250 Gm. In recent years the transthoracic approach has been the method of choice; it affords a good exposure for splenectomy. Attention should be paid to possible rupture of an aneurysm of the splenic artery. The contraindication for a transthoracic operation is traumatic rupture of the spleen, where the abdomen must be inspected for possible rupture of other organs.

Hemorrhage and Anemia in Hernias of the Esophageal Hiatus. A. Victorica. Tórax 8:25-31 (March) 1959 (In Spanish) [Montevideo].

The most frequent complications of a hiatal hernia are hemorrhage and anemia. These features can be the symptoms leading to a differential diagnosis, or they can be a serious complication, requiring an emergency operation, in patients known to have a hernia of the esophageal hiatus. The author analyzes 35 cases of hiatal hernia, in 7 of which there were evidences of anemia and hematemesis. Two of the 7 patients had profuse melena, which in one was associated with alarming hematemesis; 5 had more or less marked hematemesis. In one patient, who had come to consultation because of a general feeling of weakness, fatigue, and asthenia, the clinical and radiologic examination of the digestive tube led to the diagnosis of hiatal hernia. A typical case with anemia and hemorrhage was that of a 66-year-old woman whose initial symptoms, noticed 17 years before, had been otalgia, with irradiation of the pain to the jaws and the epigastric region. The radiologic diagnosis of hiatal hernia was established 15 years after the onset of the symptoms. Two years later the patient had a grave hematemesis with melena, and collapsed. An emergency thoracotomy was performed successfully. One year after the operation the patient was radically cured.

The author calls attention to the dangers of an undetected anemic condition and of hemorrhage of an unknown origin. He recommends that a careful radiologic examination of the esophagus with contrast mediums be performed, even during hemorrhage, whenever there is any doubt about the origin of the bleeding. Even if the patient has suffered no hemorrhage, an intense case of anemia may call for immediate operation, once the diagnosis of hiatal hernia has been established.

Hirschsprung's Disease in Infants. T. C. Jewett Jr., L. J. Leahy and J. Lanigan. A. M. A. Arch. Surg. 79:455-458 (Sept.) 1959 [Chicago].

Tardy correct diagnosis seems to have been the main reason for a high mortality rate among 26 infants hospitalized with Hirschsprung's disease. The symptoms of 12 patients up to 6 days of life were abdominal distention, vomiting, and either scant or absent passage of meconium since birth. The most frequently confused roentgenologic diagnoses were ileal atresia, meconium ileus, and midgut volvulus. Barium enema aided in differentiating the dilated large and small intestine. In Hirschsprung's disease involving the entire colon and terminal ileum, barium study showed the microcolon seen in any obstructive lesion in the newborn infant. A differentiating point was that the contrast medium was not evacuated for 24 to 48 hours in Hirschsprung's disease, while in other obstructive lesions it was promptly expelled.

The symptoms in 9 infants, between 1 week and 3 months of age, were more varied than among the younger patients. The symptoms were related to the eventual decompensation of the colon by the obstructing aganglionic segment. Six of 17 infants who underwent colostomy died; 3 of them had perforation with peritonitis, 2 had an extensive aganglionic segment, and 1 had inadequate colostomy. Also, 2 patients who did not undergo colostomy and had septicemia with visceral abscesses died. The diagnosis of Hirschsprung's disease in 5 infants, aged between 3 and 6 months, was suggested when rectal examination revealed an empty rectal segment followed by explosive foul stool on removal of the examining finger. Diagnosis of Hirschsprung's disease may be confirmed by roentgenologic examination and rectal biopsy. Colostomy is mandatory, and it is the only mode of treatment until the child is old enough for a definitive surgical correction. Temporizing measures are usually fatal.

Epiphrenic Diverticulum of the Esophagus: Surgical Treatment.

D. B. Effler, D. Barr and L. K. Groves. A. M. A. Arch. Surg. 79:459-467 (Sept.) 1959 [Chicago].

Six of 7 hospitalized patients in the 5th or 6th decade of life were subjected to surgical treatment for epiphrenic esophageal diverticulum. Pain and dysphagia were present in 6 patients, and anemia in 1. The duration of symptoms varied from less than 1 year to more than 20 years. The diagnosis was established by esophagrams. Endoscopic examination for diagnostic purpose is contraindicated because of the hazard that the esophagoscope may enter the diverticulum. Hiatal hernia, which coexisted in 5 patients, was demonstrated by diagnostic films in 3. Hypertrophy of the circular muscle of the terminal esophagus was a consistent finding. A rim or flap of esophageal mucosa adjacent to the orifice of the neck but located on the opposite side of the esophagus was present in the last 4 patients operated on; this may be a constant feature of epiphrenic diverticulum.

Of the 6 patients operated on, 5 were relieved of the symptoms with no recurrence. One patient who had severe obstruction for 20 years died on the 30th postoperative day. The surgical treatment consisted of excision of the sac; myotomy extending from the diverticulum down to the gastric wall; incision of the mucosal valve, if present, in the lumen of the esophagus; and repair of the esophageal hiatus, with complete reduction of the stomach below the diaphragm.

Adrenalectomy for Far-Advanced Breast Carcinoma.

E. M. Alrich and L. B. Brown. Virginia M. Month. 86:524-527 (Sept.) 1959 [Richmond].

Adrenalectomy, alone or combined with oophorectomy, offers significant palliation for certain patients with far-advanced carcinoma of the breast. The procedure can be accomplished with an acceptable operative risk even in patients who have not only far-advanced malignant disease but also other complicating associated organic disease. The criteria for the selection of candidates who will benefit from these procedures are not well established, but the use of certain principles predict to some extent the type of response which may be expected. The authors report on 16 female patients with far-advanced carcinoma of the breast, in whom bilateral adrenalectomy was performed as a palliative measure. Fifteen of the patients had had treatment previously, which consisted in 13 of radical mastectomy combined with roentgen radiation or oophorectomy or both; one patient underwent simple mastectomy and roentgenotherapy, one was given hormones alone, and one did not receive any treatment.

There was one operative death in this series, due to a cardiovascular accident. Nine patients, who lived from 1 to 7 months after adrenalectomy, did not have a satisfactory response to the operation. Four patients survived from 6 to more than 12 months, with evidence of both subjective and objective improvement. Two of these had predominantly bone lesions; one had both widespread bone and soft tissue metastases; and one had bone, soft tissue, and pleural metastases with pleural effusion. All 4 patients returned to their usual daily routine with few limitations. In 2 patients the operation was too recent to determine the response.

The probability that benefit will be obtained from adrenalectomy is influenced, at least in part, by the type of metastatic involvement. Liver and visceral metastatic diseases show little response, and perhaps the procedure should not be offered in this group of patients. Metastatic bone disease and soft tissue lesions are more frequently influenced in a fair percentage of the patients. If these principles are respected, this procedure can be accomplished without undue risk or sequelae and will be followed in 40% of the patients by a 6-to-12-month remission of carcinoma of the breast.

Malignant Neoplasms of the Colon and Rectum in Young Persons.

J. W. Johnson, E. S. Judd and D. C. Dahlin. A. M. A. Arch. Surg. 79:365-372 (Sept.) 1959 [Chicago].

A survey was made of the Mayo Clinic records covering a 30-year period for data on 222 patients, ranging in age from 16 through 29 years, with malignant tumor of the rectum or colon. The purpose was to search for features that would aid in differentiation of the course of the malignant disease in young patients from that in older patients. Adenocarcinoma without associated ulcerative colitis or multiple polyposis was present in 169 patients, adenocarcinoma with multiple polyposis in 27, adenocarcinoma with chronic ulcerative colitis in 25, and reticulum-cell sarcoma in 1. Resection was performed on 95 patients with adenocarcinoma, 13 of the operations being palliative. Pain was the commonest symptom in 80 patients (84%), followed by bleeding, loss of weight, constipation, and diarrhea in decreasing order of sequence. Of the 95 patients, 8 died in the immediate postoperative period, 4 died of unrelated causes, 13 died after the palliative resection, and 6 were unavailable for follow-up. Of the remaining 64 patients on whom operations were performed with a view to cure, 42 had died in less than 5 years after the operation and 2 others had died in less than 8 years. Of the 20 patients known to be still living, 8 have survived for 10 to 15 years, 6 for 16 to 20 years, and 6 for 22 to 29 years. Two patients who had survived 10 and

13 years, respectively, after resection had had small-cell adenocarcinomas; the lymph nodes were involved in one but not in the other.

The clinical features of the 95 patients with adenocarcinoma were similar to those of older patients, although pain appeared to be more prominent. The location of the lesions throughout the colon seemed to be the same in both younger and older patients, except that the rectum was involved less frequently in the younger group. Examination of the gross and microscopic pathological changes of the specimens revealed no significant differences in the age groups, but there was a higher incidence of high-grade lesions among the younger patients.

Late Edema in a Burned Patient: Study of Adrenal Functions at Different Stages in Its Course. A. Monsaingeon, H. Fouge and S. Couturier. Presse méd. 67:1505-1507 (Aug. 15 and 22) 1959 (In French) [Paris].

Recent studies in which the hypersecretion of aldosterone has been shown to be a factor in the development of cirrhotic ascites, cardiac edema, and certain edematous states accompanying severe potassium depletion may provide an explanation for the late appearance of massive edema in a 26-year-old man who suffered severe burns on both lower limbs. The lesions were comparatively limited in surface (12%), but they were deep enough to involve the muscles, bones, and tendons. The patient was in excellent general condition; his nutritional status was good; and he had no identifiable renal, cardiac, or hepatic defects. The initial replacement therapy was easily managed, and it seemed that a series of excisions and grafts would result in an uncomplicated cure after the subsidence of infection and the elimination of bony sequestra and necrosed tendons. This expectedly simple course was interrupted one month later by the appearance of secondary polyuria suggesting atypical diabetes. Elimination of this diagnosis led to a short treatment with somatotropic hormone. Edema of the lower limbs, which persisted and progressed in spite of a salt-poor diet, appeared shortly thereafter. The consequences for the burned limbs were serious: the edema, involving the raw areas and extending beyond them, interfered with the survival of the grafts, which were regularly lysed; in addition, secondary infection developed and was so severe at one time that a double amputation was considered.

The various factors usually called on to explain the appearance of surgical edema—venous thrombosis (iliofemoral or caval), heart failure, cirrhosis, renal insufficiency, amyloidosis, and denutrition—were repeatedly investigated and definitively excluded by the results of the investigative procedures. The only positive findings on which an explanation could be based were (1) the fact that the edema appeared after sudden, massive sodium depletion, (2) its persistence in spite of a salt-poor diet, and (3) its regular and cyclic development. These findings readily suggest the intervention of hyperaldosteronism, although no proof of this phenomenon can be given a posteriori by direct measurements. Indirect measurements, however, based on the study in retrospect of 390 specimens of urine obtained from the patient during the secondary period of treatment, seem to establish the part played by the adrenal glands in the development of this unusual complication. Study of the 17-ketosteroids and the 11-oxysteroids revealed complete independence between the course of the hyperaldosteronism and that of the cortisonic and androgenic activities of the adrenals. The very fact that edema developed in this case suggests that general factors of water-sodium retention were somehow brought into play. Only when these factors disappeared was control of the situation obtained and healing secured.

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A review was made of the cases of 355 patients with carcinoma of the colon during a 5-year period; diverticulosis was the associated disease in 75 patients (21%) of this series. The purpose of the study was to establish the correct procedure for an early diagnosis of carcinoma in patients with diverticulosis. The sigmoid colon was the site of adenocarcinoma in 197 patients; in 56 of them the tumor was associated with diverticulosis and diverticulitis. Change in bowel habits, constipation, flatulence, and blood in the stool were the main symptoms, in decreasing order of sequence, for suspected presence of malignancy in patients with diverticulosis or diverticulitis.

A close study was made in 35 patients with sigmoid carcinoma closely associated with sigmoid diverticula. Proctosigmoidoscopic examination of 34 patients before operation disclosed carcinoma in 20, but it was of no value for the diagnosis of diverticulosis. Barium enema inspection, which was performed on the 35 patients, revealed diverticulosis or diverticulitis in 32, and it made possible definite differentiation between carcinoma and diverticulosis or diverticulitis in 16. A presumptive preoperative diagnosis of carcinoma was made in 23 patients (65.7%). Roentgenograms resolved problematic differential diagnosis in 16 instances (45.7%). The over-all accuracy of roentgenologic diagnosis of carcinoma in 335 patients was 94%. The authors suggest prompt surgical therapy in all instances of diverticula which are suggestive of carcinoma. An annual proctoscopic and barium enema inspection is advisable in all persons having chronic colon symptoms in order to detect early a superimposed carcinoma.

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Familial intestinal polyposis is a hereditary disease with tendency toward cancer of the colon or rectum at an early age. The author describes the familial pattern of intestinal polyposis in a family of 12. The mother died of cancer of the colon when 30 years of age. The father, aged 55 years, and one sibling, aged 30, were free from intestinal polyposis at the time of study. The remaining 9 siblings had multiple polyps throughout the large intestine. A brother who was 22 years old when operated on for an obstructing lesion in the descending colon died 3 years later; at operation numerous polyps, associated with carcinoma, were seen in the colon. A sister, aged 25 years, had 2 polyps which showed malignant changes; she underwent colectomy and ileoproctostomy, and recovery was uneventful. Another brother, aged 19 years, had a single malignant polyp which was operated on. The remaining members of the family were free of malignancy but were subjected to colectomy and ileoproctostomy. All surviving patients have been followed for more than 5 years.

Three additional patients (unrelated to the aforementioned family) with multiple polyps of the large intestine, in 2 of whom the familial pattern had been demonstrated and in 1 of whom it was questionable, underwent colectomy and ileoproctostomy. Two of these patients had carcinoma of the sigmoid colon. The functional results of ileoproctostomy in all 3 patients were excellent. It seems that polyp formation was lessened after this operation, and there may even have been a regression in polyps that had appeared. Total colectomy and ileoproctostomy with fulguration, together with long-term follow-up of the polyps in the rectal stump, offer a safe procedure in the treatment of familial intestinal polyposis.

NEUROLOGY & PSYCHIATRY

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Acute ulceration of the upper gastrointestinal mucosa sometimes occurs in bulbar poliomyelitis. Two fatal cases of bulbar poliomyelitis with gastrointestinal complications are here presented. There was acute ulceration of the esophagus, stomach, and duodenum accompanied by hematemesis in the first patient. Involvement of the hypothalamus and the central autonomic pathways was thought to be the cause of the gastrointestinal ulceration. The second patient died of rupture of the esophagus. This was due to persistent vomiting and possibly incoordination of the pharyngeal muscles as a result of the brain stem lesion.

Curarization and Artificial Respiration as a Promising Therapeutic Method in Post-traumatic and Postoperative Brain Lesions with Hyperthermia. R. Brönnimann and P. Huber. Arch. klin. Chir. 291:200-211 (no. 3) 1959 (In German) [Berlin].

The authors discuss the treatment of hyperthermia that develops in patients with brain lesions as the result of either trauma or surgery. They had found that the use of artificial hibernation induced with the aid of the lytic cocktail was not satisfactory for the treatment of this form of hyperthermia. The analysis of the clinical aspects of hyperthermia revealed connections between its etiology and symptomatology. It results from the clinical concurrence of shock, cerebral and pulmonary dyspnea, and centrally induced muscular irritation; heat formation is increased, and its dissipation is made difficult as the result of the inadequate blood perfusion of the skin. For this reason the authors decided to reduce heat formation in the musculature by curarization and to improve the peripheral circulation by generous blood transfusions. The skin is a cooling apparatus, but it can perform this function only if it has an adequate, or even a slightly increased, blood perfusion. As the result of the atony of the skeletal musculature, patients with hyperthermia are in about the same condition as are patients with tetanus, who in many cases require artificial respiration and special nursing care for several weeks. Artificial respiration insures an open airway and permits the adjustment of ventilation to physiological values; furthermore, anoxia and hypercapnia can be avoided, and pulmonary complications prevented.

Before curarization is instituted, the patient should be subjected to a thorough neurological examination. In patients with brain trauma, who have only slight focal signs, cerebral angiography should be carried out, so that a still small cerebral hematoma will not be overlooked. If no hematoma is detected, curarization is first carried out with minimal doses, so that it can be interrupted should another neurological examination prove necessary. If after thorough analysis of the clinical aspects curarization and cooling seem indicated, the authors first give a blood transfusion, even if the blood pressure is increased. Then the patient is prepared for artificial respiration. If a tracheotomy had not been performed before, orotracheal intubation is carried out. To insure total relaxation, 100 ml. of succinylcholine solution is given intravenously, and then assisted breathing is begun by administering by means of the anesthesia apparatus a mixture of nitrous oxide and oxygen.

13 years, respectively, after resection had had small-cell adenocarcinomas; the lymph nodes were involved in one but not in the other.

The clinical features of the 95 patients with adenocarcinoma were similar to those of older patients, although pain appeared to be more prominent. The location of the lesions throughout the colon seemed to be the same in both younger and older patients, except that the rectum was involved less frequently in the younger group. Examination of the gross and microscopic pathological changes of the specimens revealed no significant differences in the age groups, but there was a higher incidence of high-grade lesions among the younger patients.

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Muscular relaxation is maintained by continuous drip infusion of a succinylcholine solution (1,000 mg. in 500 cc. of a 5% aqueous dextrose solution). but a dilute tubocurarine solution has also been used for this purpose. After about an hour the authors perform artificial respiration with their own manual apparatus, in which the air is saturated with steam to 98%.

The patient at first remains in bed, but if, on the basis of continuous temperature control, a more intensive cooling is deemed necessary, this is done by the use of ice water. As soon as the rectal temperature has been reduced to 36 or 37 C (96.8 to 98.6 F), the patient is dried off. As a rule, the temperature declines for another 2 or 3 C (3.6 to 5.4 F) after that. In the course of this treatment, an average of from 800 to 1,200 cc. of blood or plasma is infused. The authors gained the impression that this quantity was usually necessary for adequate cooling.

The authors present the clinical histories of 5 patients, which illustrate what curarization and artificial respiration, in combination with blood transfusion and external cooling, will accomplish in the severe hyperthermia that occurs in patients who require neurosurgical treatment. The patients were observed at the surgical clinic of the University of Bern.

Plumbism Following the Use of a Blow-Torch on Paint. J. Dorfman and M. Davis. Connecticut Med. 23:460-462 (July) 1959 [New Haven].

The authors present the history of a 52-year-old house painter in whom lead poisoning (plumbism) developed as the result of the inhalation of lead fumes which resulted from the application of a blowtorch to paint. He complained of weakness of the legs, poor appetite, and low back pain which encircled the waist and radiated into the lower abdomen. About 4 weeks prior to admission, he had developed an acute illness with generalized aches and pains and malaise, which lasted about 2 days. Shortly thereafter he had noted the onset of the symptoms mentioned above. The patient also complained of mild diarrhea with the passage of 2 watery stools daily. Plumbism was first suspected when the laboratory reported an unusual number of stippled red cells in the blood smear. The patient was then questioned about the exact nature of the work he had been doing. He said that he had recently been employed in removing several layers of paint from the woodwork of a house that was more than 100 years old. In some areas the paint was one-quarter of an inch thick, and he had used a blowtorch to facilitate its removal. Hemoglobin value, on admission, was 11.5 Gm. per 100 cc. White blood cell count and differential count were not remarkable. The blood smear showed many stippled red cells. Samples of blood and urine were submitted to a laboratory for determination of lead content. The urine contained 0.30 mg. of lead per liter (normal, 0.01 to 0.08 mg. per liter); the blood contained 0.14 mg. per 100 Gm. (normal, 0.01 to 0.05 mg. per 100 Gm.). Bone marrow aspiration disclosed hyperplasia, predominantly of the myeloid elements, with stippled red blood cells.

Medicaments included Pro-Banthine, in doses of 15 mg. 4 times a day, and Demerol, 50 mg. as needed, for relief of severe abdominal pain. Multivitamins were also given, along with a nutritional formula. Administration of small doses of saturated solution of potassium iodide was maintained for 2 weeks. The patient's symptoms gradually subsided. His stools became formed, and normal appetite returned. The backache was the last to disappear. Later in the treatment a hematinic preparation was added to the therapeutic regimen. The patient seemed sufficiently recovered to warrant discharge after 5 weeks of hospitalization. He was advised to observe the rules of safety when working with paint and to continue taking the hematinic.

Application of heat to materials containing lead or to metallic lead may result in the formation of lead fumes. Pathogenic amounts of fumes may result from burning, welding, or melting operations applied to surfaces bearing heavy coats of lead or materials containing lead.

Tofranil Treatment of Endogenous Depressions. K. Fotel-Andersen and E. Geert-Jørgensen. Ugesk. laeger 121:1091-1094 (July 9) 1959 (In Danish) [Copenhagen].

From May, 1958, to January, 1959, 100 patients (28 men and 72 women) were treated with Tofranil, an iminodibenzyl derivative, in the psychiatric department of Frederiksberg Hospital; 25 patients received ambulant treatment, and 75 started treatment in the hospital and mostly continued with ambulant treatment. Manic-depressive psychoses are 2 or 3 times as frequent in women as in men. There was no difference in the results of treatment in men and in women. In some cases Tofranil was first given as an injection, then in tablets; in other cases only tablets were given. The effect of Tofranil on emotional life in most cases appeared 16 to 18 days after the start of treatment and became maximal in the course of 1 or 2 weeks longer. No improvement was noted later than 3 weeks after the start or treatment. With few exceptions, the patients were personally reexamined by the authors. On follow-up, 45 of the 77 patients, cured or definitely improved, were under maintenance treatment; 11 had been treated for about 1 month, and 66 for an average of 4½ months. The authors' definite impression is that Tofranil exerts an excellent effect on endogenous depressions, an effect equal to, or superior to, the effect of electric shock, and on continued treatment probably reduces the frequency of recurrence. Side-effects are relatively insignificant. Treatment can be ambulant.

Cryptococcic Meningitis Treated with Amphotericin B: Case in a Patient with Histologically Diagnosed Boeck's Sarcoid. N. J. Brandt and H. Stürup. Ugesk. laeger 121:1132-1134 (July 16) 1959 (In Danish) [Copenhagen].

The mortality in cryptococcic meningitis has been between 80 and 90%. Amphotericin B seems to offer a possibility for effective treatment. Six days before hospitalization in 1958, a woman, aged 62 years, developed meningeal symptoms. On admission, there were neck rigidity and somnolence. Treatment with penicillin, sulfacombin, and Duo-Strep was without avail. After 3 weeks Cryptococcus neoformans was isolated from the cerebrospinal fluid. Amphotericin B was administered intravenously in doses of from 17 to 50 mg. daily until a total of 517 mg. had been given. The condition cleared up rapidly, and the cerebrospinal fluid became sterile. The only side-effect was nausea. The cerebrospinal fluid remained sterile 3½ months after treatment, but there has been increasing dyspnea, and roentgenologic examination shows infiltration of the lungs. The patient will be kept under observation, with special attention to pulmonary changes.

Tuberculous Meningitis: Prognosis and Treatment. B. F. Voljavec, S. P. Orton and R. F. Corpe. Am. Rev. Resp. Dis. 80:388-397 (Sept.) 1959 [New York].

The authors studied the prognostic significance of signs and symptoms as seen early in patients with tuberculous meningitis before the disease was affected by chemotherapy. Fifty-six patients with active tuberculous meningitis, 37 of whom had received no previous treatment, were given isoniazid early in the course of treatment. In addition to isoniazid, the patients received streptomycin or PAS. Seventeen patients had also received corticosteroid hormones, and one, corticotropin. Twelve of the 56 patients died.

Several factors that appeared to influence the final outcome in each case were considered separately and simultaneously. Early treatment, except for the mild stage of the disease, was the most important factor influencing prognosis favorably. Only 2 of 26 patients who were started on treatment within 7 days of the onset of symptoms died, although 14 were already in the moderate or severe stage. Four of the 14 patients who were started on treatment between 7 and 14 days after the beginning of symptoms and 6 of 15 patients who were started after 14 days of symptoms died. Factors with an unfavorable effect on the prognosis were (1) advanced stages of meningitis, particularly coma and severe focal neurological signs, (2) high-protein levels and low-sugar values in the cerebrospinal fluid, and (3) negative skin reaction to tuberculin in the face of advanced disease. There were 13 patients with complete or partial cerebrospinal block. Nine of these patients received corticosteroids, and 8 survived, while all 4 patients treated with antimicrobials alone died.

The 44 surviving patients were followed up for from 7 to 67 months. Thirty-seven of the 44 patients presented no clinically detectable residuals; in one patient the damage was considered to be moderate. Five patients survived the disease with severe and probably permanent damage. Three of these patients were from the previously untreated group, and 2 from the previously treated group. All 5 patients had severe focal neurological signs on admission, and in all of them the consciousness was disturbed; however, none were comatose. All but one of the 5 patients had been ill for more than 10 days prior to initiation of treatment, and none had received corticosteroid hormones; none showed evidence of cerebrospinal block.

Infectious Neuronitis (Guillain-Barré Syndrome) in Children. A. F. Peterman, D. D. Daly, F. R. Dion and H. M. Keith. Neurology 9:533-539 (Aug.) 1959 [Minneapolis].

The authors report clinical observations, results of laboratory examinations, and data concerning the course of illness in 19 boys and 7 girls, between the ages of 16 months and 15 years, with infectious neuronitis, who were seen at the Mayo Clinic between 1945 and 1957. In 18 of the 26 patients the disease occurred before the age of 8 years. Antecedent infection had occurred in 18 patients, although in some this may have been coincidental. Progressive symmetrical muscular weakness was the chief complaint. Involvement of muscles of the limbs occurred most often; however, muscles innervated by cranial nerves were affected in 11 children (45%). Areflexia was present in all the patients at some time during the illness. Although sensory disturbances were not common, impairment in perception of vibration and proprioception was found in 7 patients. Examination of the cerebrospinal fluid in 25 patients revealed albuminocytological dissociation in all but one patient, the protein content attaining its highest level 10 to 25 days after the appearance of clinical symptoms. Electromyographic examinations revealed features compatible with the involvement of lower motor neurons or peripheral nerves in the 10 patients so examined. Reduction in conduction velocity of peripheral nerves was a frequent observation, particularly after the first month of illness.

Seventeen patients recovered from neuronitis, showing no residual neurological deficits despite the fact that the course of the disease was prolonged in 11 of them. Complete recovery occurred within 6 months to 3 years. Two patients had relapses; seven had persistent weakness and atrophy of distal muscles of the legs 3 to 5 years after onset of their disease; one died of pneumonia, secondary to weakness of the muscles of respiration; and one was lost to follow-up. Problems in differential diagnosis are important as neuronitis may be confused with poliomyelitis, muscular dystrophy, or polymyositis.

Incidence of Ventricular and Subarachnoid Filling in Fractional Encephalography. J. L. G. Oller and P. Tartell. South. M. J. 52:1041-1047 (Sept.) 1959 [Birmingham, Ala.].

The authors report on 55 patients, between the ages of 17 months and 43 years, who were subjected to fractional encephalography on the neurosurgical service of the U. S. Naval Hospital, Camp Lejeune, N. C. The final diagnoses made were generalized epilepsy in 10 patients, focal epilepsy in 8, post-traumatic encephalopathy in 11, retrobulbar neuritis in 5, multiple sclerosis in 4, postinfectious encephalopathy in 3, tumor in 2, cerebral atrophy in 2, subdural hematoma in 1, and miscellaneous conditions in 9. Adequate ventricular filling was obtained in 54 of the 55 patients. Filling of the subarachnoid spaces was attempted in 50 of the 55 patients, and controlled and selective filling of the basilar cisterns and convexity was possible in most of them. There was filling of the anterior cisterns in 49 patients (98%), filling of the cisterna ambiens in 41 (82%), filling of the cerebellar cisterns in 44 (88%), and filling of the convex spaces in 41 (82%).

The disadvantages of the procedure are the time consumed in performing the examination, the constant attention of the neurosurgeon and radiologist to modify techniques, and the large number of films used. The advantages are the excellent visualization of the posterior fossa, the selective filling of the area desired, the relatively little discomfort with the aid of local anesthesia, the cooperation of the patient for changes of position, and decreased headache after the procedure. As experience with the technique has increased, the results obtained have improved.

Results of Catamnestic Studies and Actual Problems in Patients with Tuberculous Meningitis. A. Liener. Beitr. Klin. Tuberk. 120:315-330 (no. 5) 1959 (In German) [Berlin].

The author reports on 158 children and 53 adults with tuberculous meningitis, who were observed and treated at the District Hospital for Tuberculosis in Natters (Tyrol, Austria) between 1948 and 1958. Of the 158 children, 102 were discharged from the hospital as improved, and so were 30 of the 53 adults. Follow-up examinations showed that 94 of the 102 children and 29 of the 30 adults were alive early in 1959. Up to April, 1948, i. e., up to the time when streptomycin became available for treatment, all patients who had been admitted to this hospital for the treatment of tuberculous meningitis had died. The observations made on the 210 patients have justified the present method of treatment, which consists of the intrathecal and intramuscular administration of streptomycin combined with the oral or intramuscular administration of isoniazid preparations. In contrast to other workers, the author strongly believes that, instead of omitting the intrathecal treatment completely, it should be continued for only 8 to 12 weeks in accordance with the cerebrospinal fluid findings; except for that, the biochemical treatment should be continued for long periods. In addition, treatment with glucocorticoids should be given to all those patients in whom early diagnosis may be excluded by the general condition, case history, or cerebrospinal fluid findings.

In contrast to the view advocated in the world literature that tuberculous arachnitis occurs as a sequel to intrathecal treatment, this condition was observed only in patients who had survived as a result of biochemical-antibiotic general treatment but who had not received early intraspinal therapy. This observation justifies the author's opinion that it is not permissible to omit local therapy in patients with tuberculous meningitis, in whom treatment is instituted late in the course of the disease. Among damage caused by the therapy, there were observed impairment of the 8th cranial nerve, occurrence of a spinal epidermoid caused by trauma, and occurrence of purulent meningitis in the course of intrathecal treatment for tuberculous meningitis. Lumbar puncture, however, was not associated with noteworthy risk, complications, or side-effects.

The highly unfavorable prognosis previously attached to tuberculous meningitis has become much more favorable since the advent of streptomycin, isoniazid preparations, and glucocorticoids. In patients with severe disease and late institution of treatment, additional treatment with glucocorticoids may improve the prognosis only with regard to the prolongation of life. Furthermore, it may be associated with the increased risk of such defects as internal hydrocephalus with loss of personality, impairment of the temporal lobe with partial atrophy of the optic nerve, and basal cerebral impairment with tetraplegia.

GYNECOLOGY & OBSTETRICS

Incidence of Hypertension After Pregnancy Toxaemia. G. B. Gibson and R. Platt. Brit. M. J. 2:159-162 (Aug. 15) 1959 [London].

In an attempt to establish whether permanent and significant hypertension is a frequent sequel to a toxemic pregnancy in women who enter pregnancy with normal blood pressure, and to ascertain the amount of damage which may be done by a toxemic pregnancy in a woman already hypertensive, the authors reexamined 446 women who 4 years previously had a toxemic pregnancy and in whom the blood pressure was found to be below 140/90 mm. Hg (preeclamptic toxemia) during or before the 20th week of pregnancy (toxemic series). Also reexamined were 92 women in whom the blood pressure was found to be 140/90 mm. Hg or more during or before the 20th week of pregnancy (hypertensive series). The results of the reexaminations of the women, whose blood pressure early in pregnancy was normal, clearly showed that their mean blood pressures about 4 years after the toxemic pregnancy were much higher than the mean pressures which would be expected in an unselected population of women of similar age. Nevertheless, severe hypertension was a rare sequel of toxemic pregnancy in a previously normotensive woman. Similarly, in women who had toxemic pregnancies superimposed on hypertension, the rise of blood pressure on reexamination was more than could be accounted for by an increase of age of about 4 to 5 years.

Acute Renal Failure in Pregnancy. R. C. Knapp and L. M. Hellman. Am. J. Obst. & Gynec. 78:570-577 (Sept.) 1959 [St. Louis].

Among the 32,000 deliveries and the 10,950 cases of abortion recorded at the Kings County Hospital, Brooklyn, N. Y., between 1951 and 1958, there were 23 patients who developed acute renal failure, i. e., reduction of the urinary output to less than 50 cc. in a 24-hour period. Twelve of these 23 patients survived. Whether renal failure is caused by sepsis, incompatible blood transfusions, chemical poisons, or hypotension, the management remains the same. A successful outcome is primarily dependent on the extent of the initial kidney damage and on careful management, including a strict control of intake and electrolytes in relation to the output. Recording of the patient's weight and determinations of serum carbon dioxide, potassium, and urea nitrogen should be made daily, with the administration of sodium lactate at the first signs of fall of the carbon dioxide level. The administration of resins is indicated on rising of the potassium level. Blood replacement, in the form of packed cells, is given only if the hemoglobin level falls below 5 Gm. per 100 cc.

A case of acute renal failure after an induced abortion is reported as an example of the physiological approach to the management. The patient, a 29-year-old woman who had induced abortion with a Lysol douche, had vaginal bleeding and crampy abdominal pain. On admission, her blood pressure was 80/40; the pulse, 120; and the temperature, 101 F (38.3 C). The patient was given 500 ml. of whole blood, with stabilization of the blood pressure at 110/70. Aproximately 24 hours later the patient aborted a 15-cm. fetus with an intact placenta. For the next 24 hours the blood pressure could be maintained only with arterenol. The urinary output was only 34 cc. during that period, and contained many kidney cells and many red blood cells. The intake was reduced to 900 ml., the administration of arterenol was gradually discontinued, and 30 million units of aqueous sodium penicillin per 24 hours were given intravenously, together with 1 mg. of streptomycin given intramuscularly. As the patient entered the oliguric phase of renal failure, the administration of penicillin was discontinued and replaced by 700 ml. (plus the output) of 10% dextrose in water. A high-fat, high-carbohydrate, low-protein diet was instituted, which was poorly tolerated. On the 7th day, as the carbon dioxide content fell to 12.5 mEq. per liter, 100 ml. of molar sodium lactate solution was given. From the 11th to the 15th day, after the carbon dioxide content rose to 20.5 mEq. per liter, the patient received a carboxylic-acid-type sodium salt exchange resin, which was given in retention enemas because of repeated vomiting. After 12 days of the oliguric phase, the patient entered the diuretic phase and began to urinate more than 200 cc. per 24 hours. Intravenously administered fluids were ordered, and isotonic sodium chloride solution was given to maintain the electrolyte balance. The patient was discharged after 33 days of hospitalization. All blood chemical examinations were normal, but the specific gravity of the urine remained fixed.

Cervical Carcinoma: Cancer Cells in the Circulating Blood. A. W. Diddle, J. Hollingsworth and S. Kinlaw. Am. J. Obst. & Gynec. 78:582-585 (Sept.) 1959 [St. Louis].

Venous blood from 14 patients with invasive cervical carcinoma and from 8 patients without malignancy was examined for the presence of atypical cells. Specimens of blood were taken above the bifurcation of the iliac vein in all the patients; in some of them it was also taken from the external iliac, femoral, and antecubital veins. From each patient, 1 to 4 different specimens were studied, on the same day or at intervals of a few weeks. Tumor cells were isolated in 2 steps. The erythrocytes were removed first, by accelerated sedimentation; then the leukocytes, by centrifuged subfractionation. The sediment was fixed on glass slides and prepared by the Papanicolaou technique.

Only one of the 14 patients with cervical carcinoma had received treatment (irradiation, some months previously). Tumor cells were found in one of the 2 patients in the clinical stage 1 of the disease, in 2 of the 4 patients in stage 2, in the 2 patients in stage 3, and in 3 of the 5 patients in stage 4. The patient in stage 0 and the 8 patients without malignancy were free from atypical cells in the blood. The tumor cells were usually found alone, seldom in clumps, and only above or at the bifurcation of the common iliac vein. Their morphology was comparable to the morphology of the cells from the primary tumor. The findings indicate the association of advanced lesions with tumor cells in the circulating blood, and they raise the question of whether this correlation has a prognostic value.

Results with Wertheim's Operation With and Without Lymphadenectomy. H. Rauscher and J. Spurny. Geburtsh. u. Frauenh. 19:651-655 (Aug.) 1959 (In German) [Stuttgart, Germany].

The authors report on a total of 315 patients with carcinoma of the cervix uteri, 158 of whom were subjected to Wertheim's operation without removal of the lymph nodes, and 157 of whom underwent the same operation with removal of the lymph nodes. The operations were performed on those in the first group between 1947 and 1950 and on those in the second group between 1950 and 1953 at the women's clinic, University of Vienna. All the patients received roentgenotherapy postoperatively. The follow-up after 5 years or more showed that in stage 1 of the disease a relatively complete cure was obtained in 81.81% of the 88 patients who were subjected to radical hysterectomy without lymphadenectomy, as compared with 87.37% of the 95 patients who underwent the same operation with lymphadenectomy. In stage 2 of the disease, the comparable percentages were 66.17% of 68 patients, and 58.03% of 62 patients. The proportion of permanent cures obtained in the group in which the lymph nodes were not removed was 74.05%; in the group in which the lymph nodes were removed, it was 75.79%.

Acquired Hypofibrinogenaemia in Pregnancy. N. S. Beischer. M. J. Australia 2:180-183 (Aug. 8) 1959 [Sydney].

The majority of transient blood coagulation defects complicating pregnancy and the puerperium are due to acquired hypofibrinogenemia. At the Royal Women's Hospital, Melbourne, the clot observation test, described by Weiner in 1950, has been adopted for the diagnosis of critical hypofibrinogenemia. Approximately 5 ml. of blood is withdrawn, usually from the brachial vein, and is allowed to stand, uncitrated, in a test tube. The blood is observed during the following hour. This clot observation test is performed immediately after admission on all patients with antepartum hemorrhage or with known fetal death in utero. Critical hypofibrinogenemia is diagnosed if a normal clot fails to form within 20 minutes, or if a clot forms and subsequently dissolves.

The clotting test provides the following clinical data: 1. A stable clot indicates that the plasma fibrinogen level exceeds 150 mg. per 100 ml. 2. Partial clot dissolution indicates a fibrinogen level of between 100 and 150 mg. per 100 ml. 3. A fragile, rapidly-dissolved clot indicates a level of 60 to 100 mg. per 100 ml. 4. Absence of clot formation indicates a fibrinogen level below 60 mg. per 100 ml. All patients in groups 2, 3, and 4 have critical hypofibrinogenemia and are treated with fibrinogen. The present routine is to give an initial dose of 8 Gm. of fibrinogen intravenously. This dose restores the clotting time to normal in most cases. Even with early diagnosis and prompt fibrinogen treatment, blood transfusion is almost always necessary.

There has been no maternal death due to hypofibrinogenemia at the Royal Women's Hospital since the routine management of hypofibrinogenemia, outlined above, was adopted in December, 1955, and all 20 patients with this condition diagnosed since then have been delivered vaginally. Critical hypofibrinogenemia, although an obstetric emergency, is not as dangerous to the mother as has been reported, and it is doubtful whether cesarean section, hysterotomy, and especially hysterectomy are necessary. Critical hypofibrinogenemia may develop after normal deliveries, hence the importance for routine clotting tests to be performed in all cases of moderate or severe postpartum hemorrhage. This may particularly apply when labor has been induced by the use of oxytocic drugs. Fibrinogen and blood transfusion therapy must be instituted as soon as diagnosis permits.

PEDIATRICS

Catamnestic Observations in Patients Who Had Neuraxitis After the Onset of Measles and Who Were Treated with Glucocorticoids. A. Terragna. Minerva pediat. 11:751-756 (July 28) 1959 (In Italian) [Turin, Italy].

Eleven children, aged between 6 and 13 years, who had neuraxitis after the onset of measles, were followed up for possible psychic disorders for from 14 to 26 months. Brain symptoms appeared 2 to 10 days after the rash had developed. The patients received either of the glucocorticoids, cortisone and prednisone, in combination with antibiotics, analeptics, and sedatives. Therapy with the glucocorticoids was instituted for 1 or 2 days in 10 patients and for 3 days in 1 patient after the onset of neuraxitis. The daily dose of cortisone ranged from 60 to 150 mg., and that of prednisone from 15 to 40 mg.

The follow-up investigation consisted of neurological and psychological examinations of the children. Inquiry might also be made of their teachers as to their mental aptitudes and any possible mental disorders observed. General objective examination showed nothing significant. The neurological examination revealed a slight tendinous hyperreflexia in 4 children, one of whom also had Gordon's reflex and a winking tic. The psychological examination revealed normal behavior in all but 2 children, in whom a slight degree of irritability and of psychomotor restlessness was present. One of the 2 affected children had a slight impairment of certain mental functions. Glucocorticoid therapy was demonstrated in this series to be an effective means for preventing the development of tardy sequelae (particularly psychic) to the neuraxitis which occurs after the onset of measles. It seems that a prompt institution of such therapy for sequelae is more important than the duration of the acute phase of neuraxitis.

Essay on Certain Problems Posed by the Kernicterus of Hemolytic Disease of the Newborn. M. Lacomme, T. Boreau and C. Leconte des Floris. Presse méd. 67:1383-1384 (July 11) 1959 (In French) [Paris].

Statistics accumulated during the last 4 years show that 36 deaths, 20 of which were intrauterine, occurred among 221 infants with hemolytic disease due to anti-Rh isoimmunization born in the hospital. The reduction of the deaths in utero to 9%, as compared with the earlier figure of 36.8% in children previously born to multiparas in the same series, was the result of wide application of the principle of induced premature delivery adopted by the authors. The postnatal mortality figure of 8% (16 infants) was calculated on the whole number of infants (201) born alive, i. e., those who took at least one breath after birth. These 201 children included 141 who were born prematurely as a result of induced delivery. Kernicterus developed in 4 of the 185 surviving infants, probably because of difficulties and uncertainties encountered in early attempts to apply Mollison's rule, which fixes the safe level of bilirubinemia between 18 and 20 mg.%. All 4 cases occurred during the first 3 years of this study. The number of children with kernicterus who were born outside the hospital and brought to it only after the level of bilirubinemia had become fairly high was 3 times as great as that of the infants born in the hospital and treated by exchange transfusion within a suitable period (10 out of 177, or 5.6%, as against 4 out of 185, or 2.2%). These statistics show that confidence in the possibility of prophylaxis is justified, but they do not present a complete solution to the problem of kernicterus.

The first question to be considered is: Which neurological signs should be regarded as characteristic of kernicterus? Several years of systematic observation of the signs that might reveal the neurological state of newborn infants with hemolytic disease, almost all of whom had exchange transfusions in the first hours of life, have convinced the authors that some are commonplace, because they occur in many newborn infants and are attributable to cerebral edema or meningeal hemorrhage, while others appear to belong peculiarly to kernicterus, because they are predominant and, when associated, seem to distinguish the indisputably kernicteric syndromes from other neurological pictures. These are (1) nuchal hyperextension and (2) athetotic movements in the first days. Nuchal hyperextension is a manifestation of that hypertony which has been said to be the most characteristic sign of kernicterus. The athetotic movements, which may easily pass unobserved unless the child is under constant scrutiny, appear only at long intervals and are more or less fleeting. They are believed by the authors to have great diagnostic value.

The second question is: Should all the infants who exhibit these signs be regarded as having kernicterus? The records of the 94 children born in 1955 and 1956 were reviewed in an effort to answer this question. The 2 signs were more or less evident at some time or other in 18 of the children—excluding 3 in whom kernicterus was unquestionably present. No sequelae of any kind appeared in any of the 18, although 15 are believed to have had incomplete or atypical forms of kernicterus. No definite answer can, therefore, be given to the question, and it seems probable that the boundaries of the disease will remain uncertain until the diagnostic criteria are better defined.

It can, however, be said that kernicterus due to hemolytic disease is not necessarily or constantly followed by sequelae. The number of infants with kernicterus who recover completely with no ill-effects was formerly thought to be very small, but thanks to recent advances in therapy this opinion is now open to question.

Whooping-Cough Immunization: Clinical Follow-Up of First Barking Field Trial, 1955. V. Spiller and L. B. Holt. Brit. M. J. 2:174-175 (Aug. 15) 1959 [London].

The authors report the results of a clinical follow-up of 650 infants who were inoculated against diphtheria and pertussis in early infancy and were divided into 2 groups. One group of 315 infants ("separate" group) received 3 doses of whooping-cough vaccine at monthly intervals, followed by 2 doses of purified diphtheria toxoid precipitated by aluminum phosphate (PTAP). The other group of 335 infants ("combined" group) received 3 doses of combined diphtheria formol-toxoid and whooping-cough vaccine. In the subsequent 3 years no significant difference was found in the incidence of undoubted whooping cough in the 2 groups. Since, however, whooping cough developed in 22 children some 19 months after the end of primary immunization, administration of a booster dose at the age of 15 to 18 months seems to be recommended. As whooping cough is a more serious disease in very young infants, it might be thought advisable to give the first injection of the vaccine at the age of 2 months, or even at a younger age, in view of the

tuberculosis was probably significant. There was *no significant* difference in deaths from cancer or in deaths from all other causes.

In the case of cardiovascular-renal deaths, the excess is best explained as the result of a combination of factors involving the selection of certain physical types for this work, the increase in overweight in this group, the lack of regular physical activity, and the subjection of these persons to occupational conditions that impose strain on the cardiovascular system. Although occupational factors do not, in themselves, cause cardiovascular-renal disease, they may aggravate any such existing disease. That the age group 50 to 59 showed the greatest excess of cardiovascular deaths among firemen is attributed to the fact that in this age group are likely to be found the greatest number of persons with cardiovascular systems that react unfavorably to strenuous physical exertion or to bouts of asphyxia. The reduced mortality from tuberculosis and from respiratory diseases may be explained on the basis of careful medical selection and supervision of city firemen.

THERAPEUTICS

Oral Treatment of Diabetes Mellitus with Biguanide Derivatives: First Report. I. Schilling. Ztschr. ges. inn. Med. 14:705-711 (Aug. 1) 1959 (In German) [Leipzig, Germany].

The author reports on 80 patients with diabetes mellitus, who were treated with N'-beta-phenylethylbiguanide given by mouth for short periods in a nursing home for diabetic patients. Of the 80 patients, 39 were aged less than 40 years, and 54 had a normal body weight or were underweight. The 80 patients required an average daily dose of 36 units of insulin. Treatment with phenylethylbiguanide was started with a daily dose of 100 mg. in 2 divided doses; the dose was increased later to 150 mg., and only in some patients was it increased to 250 mg. Seventy-six patients received the drug for an average period of 8 days, 2 patients were given the drug for 4 to 6 weeks, and 2 were discharged on biguanide therapy and followed for 7 months. The change from insulin therapy to biguanide therapy was carried out by first giving combined treatment with insulin and biguanide and by gradually reducing the dose of insulin. In those patients who had been controlled with tolbutamide before the institution of biguanide therapy, biguanide was substituted at once for tolbutamide.

Twenty-six (32.5%) of the 80 patients showed a satisfactory response to biguanide. Forty-eight patients (60%), however, did not tolerate the drug well; intestinal disturbances, with lack of appetite, nausea, vomiting, and diarrhea, made continuation and evaluation of therapy quite difficult in these patients. In one patient a life-threatening condition developed, with a high degree of muscular weakness and vomiting of bile-containing fluid, a rise of rest nitrogen to 148 mg. per 100 cc., increase in amount of sugar in the urine to 81.2 Gm. per day, azotemia up to 16 mg. per 100 cc., and 16,800 leukocytes per cubic millimeter. These abnormal values were restored to normal within 3 days after withdrawal of the drug, but the muscular weakness subsided very slowly. The author, therefore, cautions against substituting biguanide therapy for insulin or tolbutamide therapy in ambulatory patients.

The results obtained showed a dependence of the responsiveness to the drug on the patient's age at the time the diabetes mellitus became manifest, the insulin requirement, the patient's age at the institution of biguanide therapy, and the duration of preceding insulin therapy. The obese patients responded better than those with normal weight or those who were underweight. A comparison of the results obtained with biguanide with those produced by the hypoglycemic urea derivatives (carbutamide [BZ 55] and tolbutamide [D 860]) showed qualitatively the same regularity. A quantitative comparison of the 2 types of drugs was not possible because of the differences in the types of patients. The clinical impression suggested a better effect of biguanide on the blood sugar level, but this observation could not be unequivocally confirmed by figures. Although the biguanide derivative is not suited for ambulatory treatment, one should not oppose further development of this therapeutic method.

Chemotherapy of Disseminated Carcinoma of the Breast. J. C. Wright, J. P. Cobb, F. M. Golomb and others. Ann. Surg. 150:221-240 (Aug.) 1959 [Philadelphia].

The authors report on 67 women, between the ages of 31 and 79 years, with incurable disseminated carcinoma of the breast, in whom 98 therapeutic trials with one, or several, of 5 chemical agents in succession were carried out at the Bellevue and University hospitals in New York. The chemical agents used were triethylenethiophosphoramide (TEPA), chlorambucil (Leukeran, CG 1348), the aminonucleoside of the antibiotic puromycin, actinomycin D, and amethopterin (Methotrexate). Mastectomy had been initially performed on all the patients, and irradiation therapy preceded chemotherapy in 65. Hormone therapy had been administered to 31 patients, and chemotherapy with other agents had been given to 30. Triethylenethiophosphoramide was given to 36 patients, chlorambucil to 6, the aminonucleoside of puromycin to 6, actinomycin D to 14, and amethopterin to 36. The duration of the treatment with these agents varied from one day to one year and 9 months.

fact that those immunized at 2 months appeared to be as well protected as those whose first injections were given at the age of 3, 4, or 5 months.

Exchange Transfusion in Newborn Infants: Experience in a Hospital Environment. A. Zanini and G. Conca. Minerva pediat. 11:762-765 (July 28) 1959 (In Italian) [Turin, Italy].

Exchange transfusion through the umbilical vein was performed in 15 hospitalized newborn infants with high serum bilirubin level during a period of one year. The transfusion was made in instances in which bilirubinemia reached the level of from 18 to 20 mg. per 100 cc. Citrated blood obtained from the donor immediately before the transfusion was used. The assistance of a surgeon for exposing the umbilical vein for catheter insertion was required only in the first operation. The insertion of a plastic catheter into the umbilical vein from the base of the umbilical cord was made in the subsequent 14 patients without the assistance of a surgeon. Cannulation was made by using a catheter smaller in diameter, which opened the way to one larger in diameter. By this procedure exchange transfusion could also be carried out in smaller hospitals. The use of blood obtained from the donor immediately before the transfusion, a slow speed of exchange, a constant control of the body temperature, and a careful manipulation with the catheter seemed to prevent the development of severe side-effects. A slight disturbance of the respiratory rhythm occurred in a few instances; this was corrected by discontinuing the transfusion for a few minutes and administering oxygen.

Left Ventricular Hypertrophy Syndrome in Infancy. S. Blumenthal and S. O. Sapin. Dis. Chest 36:179-188 (Aug.) 1959 [Chicago].

In infants a group of cardiac lesions exist which produce cardiac enlargement, predominantly of the left ventricle, without the presence of significant murmurs or central cyanosis, and in which there is a tendency to the development of heart failure. Under these circumstances the electrocardiogram may be normal or may reveal evidence of myocardial anoxia or of left ventricular hypertrophy. The authors call this complex the left ventricular hypertrophy syndrome and describe its characteristics, differential diagnosis, and treatment. This syndrome does not include more commonly occurring cardiac anomalies which produce left ventricular hypertrophy associated with significant murmurs. It does include (1) primary endocardial fibroelastosis; (2) predominantly myocardial disorders, such as (*a*) idiopathic or aseptic myocarditis, (*b*) glycogen storage disease of the heart, (*c*) tumors of the heart, and (*d*) nutritional deficiency states causing myocardial dysfunction; and (3) disorders resulting predominantly in abnormalities of coronary blood flow, as (*a*) anomalous origin of the left coronary artery and (*b*) coronary occlusive disease.

Electrocardiographic criteria of left ventricular hypertrophy are difficult to establish in infancy. The absence of the criteria for right ventricular hypertrophy in an infant with an enlarged heart is, therefore, of considerable importance. Under these circumstances it is believed that the vectorcardiogram is more accurate than the electrocardiogram in the first year of life. The vectorcardiographic configurations are so characteristically dissimilar after the neonatal period that one can easily distinguish the "normal infant pattern" from that of pathological right ventricular hypertrophy. The axis deviation, as determined from the standard leads of the electrocardiogram, is of less diagnostic value. Left axis deviation occurs not infrequently in patients with right ventricular hypertrophy and vice versa. The prognosis for survival beyond infancy is grave in these patients, and the differentiation from congenital cardiac malformations is important.

INDUSTRIAL MEDICINE

Mortality in City Firemen: II. A Study of Mortality in Firemen of a City Fire Department. E. Mastromatteo. A. M. A. Arch. Indust. Health 20:227-233 (Sept.) 1959 [Chicago].

A study of mortality was undertaken, covering the period from 1921 to 1953 in a large city (Toronto) fire department. The purpose was to find out whether firemen, when compared with other men of similar age groups, experienced any difference in mortality, particularly from cardiovascular or respiratory causes, tuberculosis, accidents, and violence. It had been suggested by some authors that occupational hazards exist in fire fighting, which cause an excess of deaths from certain causes, more particularly from cardiovascular diseases. The number of deaths from certain causes among Toronto firemen was compared with that expected on the basis of Ontario death rates for men of similar age groups. This comparison revealed a highly significant excess of cardiovascular-renal deaths among city firemen, with a reduction in respiratory and tuberculosis deaths. There was no significant difference in the mortality from cancer, from violence and accidents, from digestive diseases, from genitourinary diseases, or from all other causes.

Because of the known mortality differences in urban as opposed to rural residence, comparison was made also with city men of similar age groups for the period from 1937 to 1953. This latter comparison confirmed the highly significant excess of cardiovascular-renal deaths. In addition, there was an excess of deaths from all causes, which was statistically significant. The reduction in deaths from tuberculosis was probably significant. There was no significant difference in deaths from cancer or in deaths from all other causes.

In the case of cardiovascular-renal deaths, the excess is best explained as the result of a combination of factors involving the selection of certain physical types for this work, the increase in overweight in this group, the lack of regular physical activity, and the subjection of these persons to occupational conditions that impose strain on the cardiovascular system. Although occupational factors do not, in themselves, cause cardiovascular-renal disease, they may aggravate any such existing disease. That the age group 50 to 59 showed the greatest excess of cardiovascular deaths among firemen is attributed to the fact that in this age group are likely to be found the greatest number of persons with cardiovascular systems that react unfavorably to strenuous physical exertion or to bouts of asphyxia. The reduced mortality from tuberculosis and from respiratory diseases may be explained on the basis of careful medical selection and supervision of city firemen.

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Of the 67 patients, 48 have died, 6 have been lost to follow up, and 13 are living and under study. The results showed that, for palliation of the condition of patients with advanced disseminated carcinoma of the breast, administration of triethylenethiophosphoramide and amethopterin may be added to the classical methods of irradiation and hormonal control therapies. No improvement occurred in the patients treated with chlorambucil, the aminonucleoside of puromycin, or actinomycin D. With the use of triethylenethiophosphoramide and amethopterin, temporary regression of the disease occurred in some patients.

Combined Drug Treatment of Tuberculosis: IV. Bacteriologic Studies on the Sputum and Resected Pulmonary Lesions of Tuberculous Patients. A. D. Heaton, W. F. Russel Jr., J. Denst and G. Middlebrook. J. Clin. Invest. 38:1376-1383 (Aug.) 1959 [New Haven, Conn.].

The authors analyze the results of bacteriological studies performed on preoperative sputums and on individual pulmonary lesions of 220 patients subjected to pulmonary resection for pulmonary tuberculosis; included in these studies was drug-susceptibility testing of tubercle bacilli from preoperative sputums and from resected pulmonary lesions of 96 patients. The bacteriological findings also were correlated with the drug-treatment regimens used at the National Jewish Hospital in Denver before and after Oct. 1, 1954, including the results of bacteriological examination of resected pulmonary lesions from 37 patients who had been treated with a high-dosage, combined-drug regimen. The latter consisted of 20 mg. or more of streptomycin per kilogram per day, in combination with 16 mg. or more of isoniazid per kilogram per day, together with 50 to 100 mg. of pyridoxine daily, aminosalicylic acid being added, when indicated, to elevate the isoniazid levels.

In 206 (93%) of the total of 220 patients, there was complete agreement on the bacteriological results of the study of the preoperative sputum specimens and of the resected tissue specimens in that the sputums and the surgical specimens were either both negative or both positive on culture. Discrepancy between the results of drug-susceptibility studies made on preoperative sputums and on resected tissue specimens was found in 2 of the 96 patients. There was a high degree of correlation (95%) between the catalase activity of tubercle bacilli recovered from preoperative sputums and the catalase activity of organisms recovered on culture of resected specimens. There was a low incidence (10%) of sputum conversion on chemotherapy among "retreated" patients excreting tubercle bacilli resistant to streptomycin or isoniazid or to both agents (patients were defined as "retreated" who had received antituberculous chemotherapy for more than 3 weeks before admission to the National Jewish Hospital). The high incidence of bacteriologically negative results in studies on resected specimens from sputum-negative patients originally on high-dosage treatment with both isoniazid and streptomycin corroborates other evidence for the effectiveness of this approach to the chemotherapy of pulmonary tuberculosis.

Experience with the Therapeutic Use of a New Sulfonylurea: N-Propyl-N′-(*p*-Chlorobenzenesulfonyl) Urea (P 607), Given Orally in Diabetes Mellitus. S. Signorelli and P. Polosa. Minerva med. 50: 2535-2542 (Aug. 18) 1959 (In Italian) [Turin, Italy].

The authors report on the effect of chlorpropamide, a new sulfonylurea compound given orally to 88 patients with diabetes mellitus for a period of 1 to 6 months. Sixty-eight patients were women and 20 were men; 73 were over 40 years of age. Before chlorpropamide therapy 48 patients had received up to 40 units of insulin, and the others more than 40 units. There were excluded from the series infantile and juvenile diabetics, patients with acidosis or coma, and patients with complications that would disturb the sugar metabolism, as might easily happen in case of intercurrent infectious disease. Most of the patients were overweight. The drug was given in a beginning dose of 2 Gm. per day, 1 Gm. after each main meal; the maintenance dose ranged from 0.125 to 0.500 Gm. per day. Seventy-two patients (81%) responded to the drug, and 16 (19%) did not respond. Only 3 of the 15 patients under 40 years of age did not respond to the drug; good results were obtained in the remaining 12 patients.

As with other sulfonylureas, the quantity of insulin that the patient had taken before switching to chlorpropamide and the time of onset of diabetes did not interfere with the therapeutic success of chlorpropamide, which in some instances was able to replace large quantities of insulin in patients whose diabetes was of long standing. Glucose tolerance tests showed that the hypoglycemic effect of chlorpropamide was greater than the hypoglycemic effect obtained with either carbutamide or tolbutamide. No toxic effect was noticed in any patient. Complaints, which in some cases required discontinuation of the treatment, were of 2 types: (1) signs of individual hypersensitivity or intolerance similar to those observed with the use of other sulfonylureas and (2) signs of specific intolerance involving the digestive tract (nausea, abdominal distention, constipation) or signs of involvement especially of the vasomotor system (neurovegetative disturbances) observed only in patients who took wine with their meals. The latter signs disappeared if the use of wine was discontinued. The reaction to alcohol was noticed in 8 of 23 patients studied, and it occurred after some concentration of chlorpropamide in the blood had already occurred, usually on the 3rd or the 4th day of treatment. The administration of 50 ml. of 8% alcohol to 20 patients over 40 years of age, who were being treated with chlorpropamide, caused in all instances a more or less marked sensation of warmth and reddening of the face, in some cases associated with vertigo. During this reaction the systolic blood pressure dropped about 10 mm. Hg and the diastolic about 5 mm. Hg, the pulse rate increased slightly, and the auricular plethysmographic wave showed a slight increase. No electrocardiographic changes were observed.

Treatment of Intestinal Amebiasis with Glaucarubin. C. Pedoya, R. Charlet, A. Savelli and others. Presse méd. 67:1481-1483 (Aug. 8) 1959 (In French) [Paris].

The authors treated 10 patients with intestinal amebiasis with glaucarubin, a crystalline glucoside extracted from Simaruba glauca. This drug had appeared very active against experimental amebiasis in animals. It is administered orally in a daily dosage of 175 to 200 mg. for from 5 to 7 consecutive days. Excellent results, with the disappearance of rectal ulcerations, were obtained in acute attacks of dysentery; good results were obtained in the diarrheic form, and, on the whole, in the functional disturbances of chronic amebic colitis. Clinical tolerance of the drug was excellent; only one patient had a few transient sensations of vertigo. Rapid improvement of the general condition was noted in several patients, in whom asthenia disappeared and appetite returned after they had taken glaucarubin for a few days. These results are in harmony with those of other workers who have noted both a high percentage of cures without recurrence and excellent tolerance for the drug in patients receiving glaucarubin.

Study of a New Diuretic by the Oral Route. S. D'Alesandro, B. J. Gurmindo and others. Semana méd. 66:231-234 (Aug. 6) 1959 (In Spanish) [Buenos Aires].

A group of 8 patients (6 with heart insufficiency, 1 with the Kimmelstiel-Wilson syndrome, and 1 with decompensated liver cirrhosis) were treated with chlorothiazide, a drug which acts on the renal tubules, blocking the reabsorption of water and electrolytes. The treatment lasted for 60 days, and the daily dose was 500 mg. every 12 hours. The 6 patients suffering from heart insufficiency were receiving cardiotonic glucosides and mercurial diuretics, and were on a low-salt diet. The diuretic therapy was replaced by the oral administration of chlorothiazide, whereas the digitalis therapy was continued.

A marked improvement in the diuresis was noticeable from the first 24 hours of treatment with chlorothiazide. Together with this change in diuresis there was a general clinical improvement, without the clinical variations which characterize sudden ups and downs in the urinary output. In the patient with the Kimmelstiel-Wilson syndrome the edema disappeared, and the arterial hypertension was appreciably reduced. The patient with atrophic cirrhosis was maintained with a stable diuresis (approximately 1,300 cc. per 24 hours) by the end of 2 months of treatment. Concomitantly, there was a decrease in the ascites and in weight. The therapy was well tolerated by all the patients, its effectiveness being continued during the whole period of study. The same dose of 500 mg. daily can be maintained in order to secure an adequate, stable diuresis.

The Sulfonamide Preparation C 17922 (Orisul): Clinical and Experimental Study of Its Use in Genitourinary Infections: Preliminary Report. G. Lacapraro. Semana méd. 66:119-121 (July 23) 1959 (In Spanish) [Buenos Aires].

A preliminary pharmacological study of sulfaphenazole (Orisul) was made with a group of 8 patients suffering from different genitourinary infections and 2 normal subjects as controls. The drug was administered in tablets of 0.5 mg. in a daily dose of 1 to 2 mg. for 2 days. Determinations of sulfonamidemia and of sulfonamiduria characterized Orisul as an antibacterial agent of rapid absorption through the intestinal mucosa, minimal acetylation in the circulation blood, marked humoral and tissue diffusibility, slow excretion, great solubility in the urine, and excellent tolerance. Orisul was administered to 50 patients with several types of genitourinary infection. There were 37 men and 13 women in this series, and their ages ranged from 18 to 87 years. The patients were classified into 3 groups (with acute, subacute, and chronic infection) according to the duration and seriousness of the disease. Accordingly, the daily doses varied from 0.5 to 3 mg. The maximal total dose was 44 mg. administered over a continuous period of 22 days. Most patients received a total dose of between 20 and 34 mg. over 2 or 3 weeks.

The tolerance to Orisul treatment was generally good. Eleven patients experienced mild side-effects, such as headache, nausea, diarrhea, and allergic cutaneous reactions. In 2 patients the reactions were serious (hypoglycemia and mental confusion respectively). These were the only cases in which interruption of the therapy was thought advisable. The results were evaluated in relation to the general condition treated and in relation to the infectious agent. There was clinical and bacteriological recovery in 22% of the patients (12% of the acute, 8% of the subacute, and 2% of the chronic states). Clinical and bacteriological improvement was observed in 64% (6% of the acute, 26% of the subacute, and 32% of the chronic cases). In 10% of the patients the drug was ineffective, and in 4% the treatment was interrupted because of side-effects. The germs most susceptible to the effects of Orisul were *Escherichia coli*, *Staphylococcus pyogenes*, and the hemolytic strains of staphylococci. Moderately susceptible were Aerobacter aerogenes and Streptococcus faecalis. The most resistant was Proteus vulgaris.

Critical Appraisal and Experience with Dextromoramide (R 875): A New Dramatic Analgesic. F. de Lara. Prensa méd. argent. 46:649-658 (March 13) 1959 (In Spanish) [Buenos Aires].

One hundred four patients, suffering from pain during acute, chronic, or postoperative conditions, were treated with dextromoramide for different periods of time. The drug was administered in the form of 5-mg. tablets, 10-mg. ampuls, and 10-mg. suppositories, in daily doses that varied from a minimum of 5 mg. to a maximum of 100 mg. The results were termed excellent (meaning total relief from pain) in 31 patients, including 12 with cancer; satisfactory (marked relief without any need for additional analgesics) in 47 patients, including 25 with cancer; and mediocre (insufficient relief and need for additional analgesics) in 18 patients. The effect was negative in only 9 of the 104 patients. The ampuls and suppositories were more effective, acted faster, and caused fewer reactions than the tablets. Side-effects were experienced by approximately 40% of the patients and consisted of neurological symptoms, such as sensation of bodily lightness, nausea, postural instability, vertigo, and vomiting. These reactions could be reduced to a minimum by taking the following precautions: administration of the drug on an empty stomach, followed by a rest period of 20 to 30 minutes, and avoidance of alcoholic beverages.

Dextromoramide has excellent synergic properties; it is very effectively combined with acetylsalicylic acid (a 5-mg. tablet of dextromoramide and a 1-mg. tablet of aspirin). No danger of drug addiction has been observed. Although it is necessary to increase the dosage for patients suffering from a chronic disease and requiring a prolonged analgesic treatment, this increase is more gradual and slower than is usually the case with other medicaments. The author considers dextromoramide superior to any other analgesic he has used in his clinical experience.

PATHOLOGY

Pathological Factors in the Prognosis of Bronchial Carcinoma Following Surgical Excision. W. J. Hanbury. Tubercle 40:257-264 (Aug.) 1959 [London].

Morbid anatomic and histological features of lung resection specimens, which had been obtained at operation for bronchial carcinoma on 81 patients, were studied to evaluate the pathological factors which might influence the postoperative prognosis. One group of 26 patients survived 5 years after surgical resection of the lung for bronchial carcinoma, but another group of 55 patients did not survive 5 years. Apart from 7 women among the nonsurvivors, all the patients were men. The most frequent site of tumor was the left upper lobe, and the patients with tumors of this lobe had the highest 5-year survival rate. The average tumor size in the survivors was 79 cc.; in the nonsurvivors it was 114 cc. This relatively small difference indicates that the size of the tumor by itself was of slight, if any, prognostic significance.

Involvement of regional lymph nodes was present in 15 patients (42%) of the 5-year survival group and in 42 patients (76%) of the fatal cases. Paratracheal nodes were found involved in 10 patients (18%) among the nonsurvivors and in none among the survivors. Squamous-cell carcinoma was found more frequently in the survival group than among the nonsurvivors. In each instance most of the squamous-cell tumors were poorly differentiated. The number of tumor-cell mitoses had no apparent bearing on prognosis and could not be correlated with the size of the tumor and the length of the clinical history. Neoplastic infiltration of adjacent structures other than lymph nodes was found in 4 patients (15%) of the 5-year survival group and in 17 (31%) of those who did not survive 5 years.

Further Research in the Isolation of Tumor Cells in the Circulating Blood. C. Colombo, F. Rolfo and G. Maggi. Minerva med. 50:2217-2223 (July 7) 1959 (In Italian) [Turin, Italy].

The arterial blood of 4 patients with nonneoplastic disease and that of 42 patients with carcinoma and of a patient with nonoperable occipital glioma was examined. The search for tumor cells was made by a method of accelerated sedimentation of the erythrocytes and preparation of smears stained by the May-Grünwald and the Giemsa methods. In each case 2 cc. of arterial blood was made uncoagulable by adding 1 cc. of Plexocrom A. Two cubic centimeters of a 5% dextran solution (molecular weight, 179.000) was added, and the container, resting at a 45-degree inclination, was placed for 30 minutes on a stove at 37 C temperature. The supernatant plasma suspension was aspirated by means of a pipette and centrifugated at 1,000 rpm for 30 minutes. This liquid was streaked on 3 glass slides which were stained with May-Grünwald and Giemsa stains. Cells believed to be of neoplastic origin were found in 7 instances. Positive findings were much more frequent among patients with carcinoma of the bronchi than among patients with carcinoma of other localizations. Four control patients gave negative results. A cell of uncertain but suggestive nature was found in a patient with immature cerebral glioma.

Cytological Examination of Sputum and Bronchial Secretion in Pulmonary Cancer. L.-G. Wiman. Nord. med. 62:1081-1084 (July 16) 1959 (In Swedish) [Stockholm].

The author has since November, 1958, tested a new staining method in exfoliative cytology, based on the occurrence of protein-bound sulfhydryl groups in increased concentration in cancer cells. The method, described by Barrnett and Seligman and later modified by Bahr, was previously used only on sections. Cells can scale off from the exterior of a tumor and be found later in secretion available for cytological examination. On microscopic examination with low-power magnification of smears from sputum and bronchial secretion, malignant cells show a distinct hyperchromasia and give an immediate conception of the size and frequency of suspected cancer cells. Study of the details with higher-power magnification confirms variations in size and form in the cytoplasm and nuclei and affords criteria for judging malignancy.

Pathogenesis of Jaundice in Hodgkin's Disease: Report of Two Cases with Hepatic Duct Jaundice. E. Mac-Clure, C. Lemos, C. S. Ferreira and M. A. Paes Leme. Hospital 56:59-80 (July) 1959 (In Portuguese) [Rio de Janeiro].

The differential diagnosis of symptomatic hemolytic jaundice and of obstructive jaundice secondary to Hodgkin's disease may be difficult, especially in cases of undetected malignant lymphogranulomatosis. The authors believe that the commonest mechanism leading to jaundice in patients with Hodgkin's disease is the biliary obstruction caused by the involvement of the intrahepatic ducts in the malignant process. They report 2 cases of obstructive jaundice associated with Hodgkin's disease observed in the pathology department of the Mercy Hospital in Rio de Janeiro. In both cases the autopsy findings showed intrahepatic duct obstruction and confirmed the causative role assigned to the involvement of the intrahepatic ducts.

The first patient was a 13-year-old boy whose symptoms started with a growth on the left side of the neck and high fever. Two months after surgical removal of the left cervical lymph nodes, there appeared another growth on the right side of the neck, which received the same treatment. The patient was readmitted to the hospital one month later because of a respiratory condition with mucopurulent sputum. The liver was palpable, tender, and hardened. Mild jaundice was present. Both the jaundice and the hepatomegaly progressed gradually and were accompanied by asthenia and anorexia. The patient died 46 days after his third admission to the hospital and 14 months after the onset of his disease. The autopsy report included a diagnosis of malignant lymphogranulomatosis with neoplastic infiltration of the portal spaces, compression and distention of periportal biliary ducts by fibrosis, and hepatic duct obstructive jaundice.

The second patient, a 25-year-old man, was hospitalized because of a growth in the left supraclavicular fossa and the presence of palpable lymph nodes in the inguinal regions, weakness, and loss of weight. His first symptom had been a growth in the left inguinal region, which was incidentally discovered in the course of an appendectomy. One month later there appeared a cervical growth, also on the left side. Under radiotherapy the inguinal tumor disappeared, and the size of the cervical tumor decreased. However, mobile tumors appeared in the abdomen, as well as splenomegaly and pain in the left leg. The treatment consisted of the administration of Sarcoclorin in a daily dose of 20 mg. during 2 days, then reducing the dosage to 15 mg. After having received 300 mg. of Sarcoclorin, the patient had gained 10 kg. (22 lb.), had no fever, and was in good general condition. This remission lasted for 2 months. Then inguinal and cervical lymph node enlargement reappeared and was accompanied by other symptoms; after another short remission, high fever and intense jaundice occurred. As there was an outbreak of viral hepatitis in the hospital ward, these new symptoms were interpreted as manifestations of the epidemic disease. Seven days later the patient died, approximately 3 years after the onset of malignant lymphogranulomatosis. At autopsy the same findings of hepatic duct obstructive jaundice, associated with Hodgkin's disease, were present as in the first case reported.

Needle Biopsy of the Liver: Analysis of 245 Cases. H. F. Rodriguez, E. Rivera, L. G. Moliner and G. Basora. Bol. Asoc. méd. Puerto Rico 51:215-227 (July) 1959 (In English) [Santurce].

Two hundred forty-five patients suffering from different types of disease, who were suspected of having a pathological involvement of the liver, underwent needle biopsy at the medical service of the Ponce District Hospital in Ponce, Puerto Rico. The largest group in this series was composed of 126 patients (approximately 50%) with intestinal schistosomiasis. There were also 25 patients with metastatic carcinoma of the liver, 19 with portal cirrhosis, 17 with viral hepatitis, 12 with obstructive jaundice, and 11 with hepatosplenic schistosomiasis. Of the remaining 35 patients, 12 showed no specific changes in the liver structure, and 23 were distributed among small groups suffering from different conditions. The biopsy was performed through a subcostal approach in the cases of marked hepatomegaly, and through an intercostal approach when the liver was not enlarged. A fragment of hepatic tissue of 1-to-2-mm. diameter and 1-to-2-cm. length was taken from each patient by a bipronged Vim Silverman needle. Frequent blood pressure and pulse determinations were performed, and sedative premedication was administered to apprehensive patients.

In the intestinal schistosomiasis group, the liver biopsy was positive in 60 patients, doubtful in 13, negative in 50, and inconclusive in 3 because of inadequate material. In the group of 25 patients with metastatic carcinoma of the liver, the biopsy confirmed the clinical diagnosis in 20 patients; in 3 it showed absence of metastases; and in 2 it established the diagnosis of malignancy, which had not given any clinical symptoms. In 13 of the 19 patients with portal cirrhosis, the biopsy confirmed the clinical diagnosis; in 4 it established the diagnosis; and in 3 the material was inadequate. In the obstructive jaundice group, 11 of the 12 patients had the diagnosis confirmed by the biopsy; in one the biopsy was negative, but the clinical diagnosis was confirmed at autopsy. In the series, as a whole, the needle biopsy was positive in 152 patients (62%), and negative in 81 (33%); in 12 patients (5%) the material was inadequate. The results indicate that the procedure can accurately sample all diffuse types of hepatic lesions, such as fatty changes, hepatitis, obstructive jaundice, cirrhosis, and a fair amount of such focal lesions as schistosomiasis, granuloma, metastases. A biopsy may, in several instances, save the patient from a laparotomy. The authors call attention to the risks involved in certain circumstances, especially if there are bleeding tendencies or symptoms of pleural disease or congestive heart failure. As the biopsy does not yield information regarding the hepatic function, an accurate diagnosis of liver disease also requires physical examination, liver function tests, and information about the patient's history.

Thesaurosis Following Inhalation of Hair Spray. B. G. Edelston. Lancet 2:112-113 (Aug. 15) 1959 [London].

The author reports on a 26-year-old woman who demonstrated cough, malaise, and loss of appetite and energy for about a year. Physical examination showed nothing abnormal in the chest. Chest radiographic appearances of bilateral hilar adenopathy and diffuse mottling mainly confined to the mid and lower zones of both lung fields proved to have been caused by inhalation of hair spray. The patient had sprayed her hair about twice daily some months previously with 2 well-known brands of fixative. She had used the spray for about 6 months and had not used it again. The provocative agent in this case may have been macromolecular synthetic resins used as a fixative, which, unlike dextran, cannot be metabolized in the body. Disappearance of the radiographic abnormalities may mean that the irritant has been removed from the lungs by phagocytosis to storage sites elsewhere; for example, to the liver or spleen. The ultimate effects of this form of thesaurosis can be ascertained only by long observation. This case is reported in the hope that physicians will recognize the possibility that in women pulmonary shadowings of unknown etiology may be due to inhalation of particulate matter from hair sprays.

RADIOLOGY

Arteriosclerotic Aneurysm of the Cardiac Coronary Arteries: Report of Two Cases. E. A. Ramirez, J. E. Taveras and J. Haddock. Bol. Asoc. méd. Puerto Rico 51:268-280 (Aug.) 1959 (In English) [Santurce].

Two cases of arteriosclerotic aneurysms of the cardiac coronary arteries, in a 32-year-old man and a 64-year-old man, are reported. There were no clues for a clinical diagnosis. The changes in the electrocardiograms showed recent myocardial infarction in the younger patient and a healed myocardial infarction in the older one. The abnormalities of the heart and the local blood vessels were not specific for coronary aneurysm. The patients died within 3 and 4 days, respectively, after hospitalization. Autopsies were performed. Two aneurysms were found in the coronary arteries of the younger man, and one in those of the older. In both cases the aneurysms had calcified walls. Both cases presented the characteristic atheromatous formation at the site of the aneurysm, diffuse calcareous deposition, disruption of the vessel wall, and diffuse arteriosclerosis of the coronary vessel. In the younger patient one aneurysm was larger than the other. The marked calcification in the wall of the larger of the 2 aneurysms of this case suggested an x-ray examination of the gross heart specimen. This film showed so clearly the calcified outline of the lesion that an effort was made to locate the lesion on the admission chest x-ray by side-to-side comparison of both films. It was interesting to find the lesion faintly outlined at the level of the third intercostal space, just to the left of the midsternal line. It could have been clearly visualized if a Bucky roentgenogram or a tomogram had been taken.

The authors recommend the use of Bucky roentgenograms in cases of suspected carotid aneurysm. The possibility of coronary aneurysm should be considered in the differential diagnosis of cardiac aneurysm versus intracardiac calcification of unknown origin.

Thoracic Aortography in Infants and Children. R. S. Cartwright and S. R. Banersfield. Ann. Surg. 150:266-274 (Aug.) 1959 [Philadelphia].

The authors performed thoracic aortography with sodium diprotrizoate (Miokon) as contrast medium in 92 infants and children, in 69 of whom a patent ductus arteriosus was suspected; 12 were thought to have simple coarctation of the aorta; 8 were thought to have coarctation of the aorta associated with patent ductus arteriosus or an interventricular septal defect; and in 1 each the aortography was prompted for aortic sinus fistula, aortopulmonary fenestration, and vascular ring. Satisfactory thoracic aortograms were made in 83 of the 92 patients and a definitive diagnosis resulted in 34 patients (41%). Of these, diagnosis of patent ductus arteriosus was made in 17 patients, coarctation of the aorta in 13 patients, patent ductus arteriosus associated with coarctation of the aorta in 2, and interruption of the aortic arch in 2. These diagnoses have been confirmed in 24 patients at surgical intervention performed for the correction of their defects, and 7 additional patients will undergo surgical treatment in the future. Of the 34 patients in whom definitive diagnoses were made, 17 were aged less than 7 months, 10 were between the ages of 7 and 24 months, and there were 7 children between the ages of 2 and 14 years. Satisfactory thoracic aortograms were made in 52 of 53 consecutive patients, without mortality, by means of a standardized technique with injection into the left carotid artery. The reported data prove the diagnostic and indirect therapeutic value of thoracic aortography in infants and children.

Myelofibrosis: The General and Radiologic Findings in 25 Proved Cases. T. F. Leigh, C. C. Corley Jr., C. M. Huguley Jr. and J. V. Rogers Jr. Am. J. Roentgenol. 82:183-193 (Aug.) 1959 [Springfield, Ill.].

The authors report on 15 women and 10 men, between the ages of 36 and 85 years, with myelofibrosis, in whom bone changes were observed roentgenographically in the department of radiology of Emory University Clinic in Atlanta, Ga., between 1948 and 1958. The diagnosis of myelofibrosis was proved by biopsy or autopsy in 24 of the 25 patients. The first symptoms were weakness and easy fatigability. The duration of symptoms before the diagnosis varied from 1 month to 16 years and averaged 47 months. The prominent physical findings at the time of diagnosis were splenomegaly, hepatomegaly, and pallor. Generally, the blood picture was one of a slight to moderate anemia with variable platelet and total white blood cell counts, associated with a leukemoid left shift of the white blood cell differential count and frequently with reticulocytosis. A striking feature was the frequently noted presence of marked anisocytosis and poikilocytosis of the red blood cells. Marrow aspiration of 21 of the 25 patients produced hypocellular preparations or blood. Progressive anemia was the major difficulty observed during the course of the disease in 17 patients. Three patients were lost to follow-up. Of the remaining 20 patients in whom the duration from the time of diagnosis could be analyzed, 10 have died, and 10 are alive. The duration from diagnosis to death ranged from 2 months to 9 years. The duration from diagnosis to the present time in those living ranged from 7 months to 12 years.

The roentgenologic findings consisted of splenomegaly in 18 patients, of hepatomegaly in 9, and of osteosclerosis in 11 patients. The osteosclerosis was diffuse rather than localized. The involved bones were not expanded, and there was no change in their external contour. The osteosclerosis was due to thickening of the individual bone trabeculae of the spongy substance, and the bones in which the changes were more apparent were the ribs, pelvis, vertebrae, clavicles, and scapulas. Changes in the metaphyseal ends of the femurs and humer were also frequently noted. Changes in the skull radius and ulna, and tibia and fibula were rarely detected in the roentgenograms. Changes in the bones of the hands or feet were not detected. In the more advanced cases of osteosclerosis, there were frequently found discrete sclerotic foci in addition to the general osteosclerosis. These foci may be present in practically all the bones involved, or limited to a few. The opinion has been expressed that the pattern of osteosclerosis seen in myelofibrosis is characteristic of the disease. When splenomegaly and osteosclerosis are present, the diagnosis of myelofibrosis can be suspected almost invariably from the routine chest examination. The splenomegaly will usually be suggested by the elevation of the left diaphragmatic leaf. This should alert one to study the bones carefully for osteosclerotic changes, which can be recognized in the thoracic bones, particularly the ribs and vertebrae.

Roentgen Findings in Histoplasmin-Positive School Children. W. M. Whitehouse, W. N. Davey, O. K. Engelke and J. F. Holt. J. Michigan M. Soc. 58: 1266-1269 (Aug.) 1959 [St. Paul].

Tuberculin and histoplasmin testing was performed on 9,400 persons from selected schools of Washtenaw County, Michigan, including incidental testing of teachers and other school personnel with whom students were in contact. Of the 9,400 subjects, 9,073 were children. An extremely high incidence of positive histoplasmin reactions was fou in the village of Milan in comparison with the surrounding communities. Nearly 90% of the school children in Milan had acquired a positive histoplasma skin reaction by the time they had reached the age of 14 years.

A total of 770 x-ray examinations were carried out in this group of 805 positive histoplasmin reactors in the Milan schools. Fourteen of the 770 films were technically unsatisfactory. Of the remaining 756, no abnormality was seen on 570 films, giving an incidence of negative findings of 75%. In 124 of the remaining 186 children with positive findings, the process had already progressed to a stage of parenchymal or nodal calcification or both. Additional findings of interest included unilateral hilar calcification as the most frequent abnormality seen, with slightly lower incidence of solitary parenchymal calcification, and a combination of these findings. Multiple parenchymal calcifications occurred less commonly than the solitary calcification. Among the earlier uncalcified lesions, hilar adenopathy, nodular lesions, and infiltrative lesions were found in roughly equal incidence. Any combination of the calcified and the uncalcified lesions might occur. Pleural involvement was relatively minor and was infrequently seen.

It is apparent from histoplasmin testing of school children that optimum microclimatic conditions are prevalent in at least one area in southern Michigan. It is entirely possible that others may be found if intensive skin testing is carried out.

Joint Infections Following Steroid Therapy: Roentgen Manifestations. R. L. Tondreau, P. J. Hodes and E. R. Schmidt Jr. Am. J. Roentgenol. 82:258-270 (Aug.) 1959 [Springfield, Ill.].

The authors report on 13 women, between the ages of 23 and 78 years, and 4 men, between the ages of 38 and 63 years, in whom joint infections developed after steroid therapy. Sixteen of the 17 patients had received intra-articular injections of hydrocortisone, and 5 of these had also received systemic steroid therapy. Pulmonary tuberculosis and tuberculosis of the hip developed during a prolonged course of orally administered cortisone therapy for lupus erythematosus in one patient who received no intra-articular injections. Of the 16 patients who were given intra-articular injections of hydrocortisone, 9 were being treated for rheumatoid arthritis, 5 for degenerative joint disease, 1 for bursitis, and 1 for lupus erythematosus. The roentgenograms of 13 patients were available for review; in 7 of these there was definite evidence of septic arthritis; in 1 there was demineralization and possible bone destruction secondary to infection. Soft tissue swelling was shown in one patient who had superficial infection but no evidence of joint involvement. In 2 patients there was evidence of the basic processes, rheumatoid arthritis and degenerative joint disease, respectively, but no evidence of septic arthritis. In both of these patients there was clinical and bacteriological proof of infection, but the processes were brought under control before roentgenologic changes occurred. Bacteriologically, hemolytic Staphylococcus pyogenes var. aureus was isolated in 11 patients, Mycobacterium tuberculosis in 1, Myco. tuberculosis and hemolytic Staph. aureus in 1, hemolytic and nonhemolytic Staph. pyogenes var. albus in 1, nonhemolytic Staph. albus in 1, and Clostridium perfringens in 1. In one patient there was definite clinical evidence of infection, but organisms could not be cultured.

It is likely that in those patients receiving only intra-articular injections the infections were caused by breaches of technique. There seems to be little doubt that in those patients who received steroids systemically these compounds played a role in the initiation and spread of infection by interfering with the normal defense mechanism of the host.

Osteoid Osteoma: A Report on 80 Cases. R. H. Freiberger, B. S. Loitman, M. Helpern and T. C. Thompson. Am. J. Roentgenol. 82:194-205 (Aug.) 1959 [Springfield, Ill.].

The authors report on 54 male and 26 female patients, between the ages of 17 months and 56 years, with osteoid osteoma, whose salient features have been tabulated, discussed, and compared with other published series of cases. Of the 80 patients, 71 were below 25 years of age. Symptoms, physical signs, and roentgenographic findings in these patients supported Jaffe's contention that the lesion of osteoid osteoma is not due to infection. The characteristic roentgenographic appearance of osteoid osteoma consists of a radiolucent center representing the osteoid nidus, surrounded by a zone of radiopacity representing the perifocal sclerotic bone. Evidence pertaining to the natural course of the disease has been reviewed, and it is concluded that surgical excision of the entire nidus is the proper treatment, since it provides immediate and permanent relief of symptoms.

Osteopathia Condensans Disseminata (Osteopoikilosis): Study of a Family of Four Generations. J. C. Melnick. Am. J. Roentgenol. 82:229-238 (Aug.) 1959 [Springfield, Ill.].

The author discovered osteopoikilosis on a routine chest roentgenogram obtained from a 42-year-old man, which led to a bone survey. Roentgenograms of the patient's 2 children (7-year-old fraternal twins) showed that only one had osteopoikilosis. These findings then led to an examination of the entire family, which included 4 generations. Roentgenograms were limited to views of the hands, wrists, feet, ankles, pelvis, and upper one-third of the femurs, since the incidence of osteopoikilosis is higher in these bones. Seventeen cases of the disease were found in 10 male and 7 female members of this family. The youngest patient was 4 years of age, and the oldest was 74. The latter patient and 3 additional patients, aged 73, 70, and 68 years, respectively, are the 4 oldest patients in whom osteopoikilosis has been reported.

The first generation represented the first reported mating of 2 persons with osteopoikilosis. The maternal side of the first generation revealed 2 additional members with positive findings. An offspring of one of these members showed a single lesion of a phalanx. There were 8 persons in the second generation, all of whom were affected. Of these, one patient also showed several exostoses; another patient had localized cortical thickening of a femur. The 3rd generation revealed 5 positive cases; a 6th member of this generation showed a single lesion in a phalanx. Of the 2 members of the 4th generation, one showed a single lesion of the femur. The cases of the persons with single lesions were suggestive of osteopoikilosis; however, in view of the paucity of the findings, it was felt that they were not diagnostic of the condition. In the event that these 3 persons represented an early stage of osteopoikilosis, there would then be a total of 20 cases in this family study, including the first reported case in a 4th generation.

Osteopoikilosis is a sclerosing osteopathy which roentgenologically may present numerous foci of small spherical or elongated sclerosis, varying from a few millimeters to several centimeters in diameter, in the spongy substance of the epiphysis and metaphysis of the bone; this is known as the nodular or lenticular type. A second type is the striated or linear type which appears as condensations along the diaphysis. The third type is a combination of the two. Genetically, osteopoikilosis appears to be caused by a dominantly inherited autosomal gene. All members of the family with the disease were heterozygotes, with one possibly being a homozygote.

Observations on the Systemic Venous Collateral Circulation in Portal Hypertension and Other Morbid States Within the Thorax. R. Schobinger, P. Cooper and L. M. Rousselot. Ann. Surg. 150: 188-195 (Aug.) 1959 [Philadelphia].

The authors performed costal intraosseous venography in 50 patients with portal hypertension not accompanied by ascites, and in 50 normal persons. The method consisted of injecting 20 cc. of a 50% solution of diatrizoate (Hypaque) sodium under constant and moderate pressure, within 5 seconds or less, directly into the medullary cavity of the 10th or occasionally the 9th rib. In the normal persons, the contrast medium rapidly passed from the medullary cavity of the rib into one or two intercostal veins corresponding to the level of injection. These veins drained into the hemiazygos vein posteriorly. This latter venous channel crossed to the right at the level of the 7th to the 9th thoracic vertebra and joined the azygos vein which could be identified up to its point of junction with the superior vena cava. The demonstrated vascular pattern was not complicated. The caliber of the respective veins remained more or less uniform, and the transition from one vein into the other was smooth and well delineated, with the hemiazygos and azygos veins well outlined by the opaque medium.

A characteristic deviation from the normal systemic venous pattern was manifested in the patients with portal hypertension. A complicated and seemingly confusing network of venous channels may replace the normal simple configuration as follows: 1. An occasional increased opacification of the costal medullary cavity. 2. An increased number of intercostal veins, usually 3 or 4, and occasionally more; these veins may appear more tortuous than normally and more densely filled with contrast medium. 3. Presence, in some instances, of venous collaterals along the thoracic and abdominal wall. 4. A variably pronounced increase in the number of small veins at the junction of the intercostal and hemiazygos veins. 5. Prominence of the junction of the intercostal, hemiazygos, and intervertebral veins. 6. Visualization of the internal vertebral venous plexus which is a conglomerate of venous channels located within the spinal canal. 7. Occasional demonstration of an accessory hemiazygos vein and of venous collaterals in the upper mediastinum. 8. Failure of visualization of the hemiazygos and azygos veins except for the bulb of the azygos vein which is regularly opacified.

After a portacaval shunt and the reduction of portal tension to sufficiently low levels, a reversion to a normal hemiazygos-azygos complex was observed. The systemic venous pattern in the patients with portal hypertension was distinctly different from that in patients with organic block (superior vena cava syndrome) or with functional obstruction (cardiac decompensation), in which the hemiazygos and azygos veins appeared always opacified up to the point of obstruction. Additionally collateral venous pathways, especially the internal vertebral venous plexus and the ascending lumbar veins, might be demonstrated, but at a lower level, i. e., along the lumbar spine.

This method roentgenographically outlined the cardiofugal direction of venous blood flow in these patients, in contradistinction to the cardiopetal direction of systemic blood flow in most of the patients with portal hypertension. The addition of costal intraosseous venography to portal portography, portal manometry, and occlusive hepatic vein pressure studies should further increase the knowledge of hemodynamics in patients with portal hypertension.

BOOK REVIEWS

Surgery of the Colon. By E. S. R. Hughes. Cloth. $12.50. Pp. 416, with 235 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 & 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

This monograph is a sequel to "Surgery of the Anus, Anal Canal and Rectum," published in 1957. The author states that he has recorded his experiences and presented his views on conditions which affect the colon. Because there are several books on the same subject, the author believes that another one is justified only if it gives an account of a personal experience, and this is what he has attempted. The unique aspect of this volume is that it presents both medical and surgical treatment of the disorders of the colon, in accordance with the author's belief that clinicians interested in gastrointestinal diseases should not be classified into groups of physicians and surgeons but rather should be in a position to treat any disease of the colon.

Chapter one describes the surgical anatomy of the colon. Chapter two presents the author's method for investigating disorders of the colon; this includes clinical examination, sigmoidoscopy, and radiologic examination. In keeping with the author's belief that diagnosis and treatment of any condition of the colon should be included, chapters three and four are devoted to chronic constipation and diarrhea. In the chapter on general principles and technique in operations on the colon, the author states that preoperative blood studies, while performed as routine by some surgeons, have not been found a feasible procedure by most and that he does not believe that the practical value of the determination has been established. He also states that estimations of serum protein and electrolyte levels have a limited value. He believes that intravenous therapy is unnecessary during operation when the right half of the colon is resected because fluid balance can be maintained in the postoperative period with rectal administration. Intravenous therapy is given for operations on the left half of the colon however. In this chapter a section is devoted to the steroid treatment of patients who have received these drugs prior to operation. It is interesting, perhaps, that the author uses chromic catgut in all layers when closing the peritoneum and rectus sheath after operation. The skin is closed with interrupted silk sutures.

The chapter on ulcerative colitis is detailed and profusely illustrated. All of the problems with respect to ulcerative colitis are considered, including the incidence of carcinoma in patients with this condition. In construction of the ileostomy, the author favors approximately the full thickness of the wall of the ileum to the edge of the skin incision. To evert the ileum and produce an ileostomy which projects, the suture can take a "bite" of the serosa at the level at which it passes through the incision in the skin. The author advises placing the sutures at less than 1 cm. apart around the edge of the ileostomy. The complications, retraction, and management of the ileostomy are also considered. The author also devotes a section to a discussion of indications for subtotal colectomy and ileorectal anastomosis.

Subsequent chapters discuss regional or segmental colitis, amebiasis, and actinomycosis. With respect to the treatment of acute colonic obstruction, the author favors a tube cecostomy as the primary procedure in most patients. He prefers performing a celiotomy through a right paramesial incision and examining the abdomen. A tube cecostomy is then constructed through the right paramesial incision or through a short incision in the right iliac fossa. The author states that while a right transverse colonic colostomy is the most effective method of decompressing the colon, its chief disadvantage is that its presence might add to the difficulty of subsequent resection. In the chapter devoted to carcinoma of the colon, the author lists the various principles governing resection of the tumor and restoration of continuity of the intestine. He points out the danger of dislodging fragments of neoplasm into the venous system during manipulation of the tumor unless the pedicle is secured at an early stage of the operation. In resection of nonobstructive carcinoma of the rectosigmoid junction, the author prefers to irrigate the rectum after the placing of a right-angled clamp. The solution used is 1:500 perchloride of mercury.

Subsequent chapters discuss benign tumors of the colon, familial intestinal polyposis, carcinoid tumors, endometriosis, and vascular disease of the colon. The book is printed on high-grade paper, contains an adequate subject index, and is generously illustrated.

Manifestaciones osteoarticulares de la brucelosis. Por J. Rotés Querol, actual jefe del Departamento de reumatología de la Cátedra de patología general del Profesor A. Fernández Cruz de la Facultad de medicine de Barcelona. Cloth. 290 pesetas. Pp. 210, with 60 illustrations. Editorial JIMS, Vía Augusta, 63, Barcelona, Spain, 1959.

In 1944 a valuable monograph on human brucellosis, written by Prof. A. Pedro-Pons and Dr. P. Farreras Valenti, was published in Barcelona. Be-

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

cause of World War II this publication did not attract the universal attention that it should have received. The present volume on the bone and joint complications of brucellosis is based on 174 consecutive cases of brucellosis studied in the clinic of Pedro-Pons in Barcelona from 1927 to 1955. This is a study of disease due to Brucella melitensis and reflects the large number of severe complications that are caused by this species of brucella as compared to those caused by Brucella abortus. This valuable contribution presents details of the clinical, roentgenologic, and pathological aspects of Brucellosis. Each chapter has an English summary. The author emphasizes the rarity of chronic rheumatoid disease involving the peripheral joints, as a complication of brucellosis, and stresses the commonly associated finding of spondylitis and sacroiliac disease. The reproductions of roentgenograms in this monograph leave much to be desired. The bibliography is restricted in scope and does not include some of the more recent studies that have been made in the United States and South America. Nevertheless, this monograph reflects a rich clinical experience with brucellosis. The observations are unusually objective and the conclusions are based on close observation of the disease. The book can be recommended as a definitive and reliable work that should be helpful to all physicians interested in the subject.

Ciba Foundation Symposium on the Regulation of Cell Metabolism. Editors for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., and Cecilia M. O'Connor, B.Sc. Cloth. $9.50. Pp. 387, with 109 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, 1959.

To biochemists the basic systems controlling cellular metabolism are to be found within the cell itself; such factors as hormones and the nervous system are thought to superimpose their action on these basic systems. This symposium is a discussion by experts for experts—as the preface points out—of nonhormonal regulations of cellular chemistry. The theme is well stated at the outset by the symposium chairman, Sir Hans Krebs. He says: "It is probable that regulation of metabolism operates always through variations of reaction velocities. . . . One of the main problems in the analysis of regulation is the identification of those component reactions which are rate-limiting." This leads into brilliant and authoritative presentations of such subjects as the control of rate of intracellular respiration, quantitative aspects of the control of oxygen utilization, control of oxidative phosphorylation, choice of oxidative pathways of carbohydrate metabolism, alternative pathways of electron transport, limiting factors in glycolysis, phosphate turnover and the Pasteur effect, enzymic regulation of fermentation, mechanisms for control of enzyme synthesis, and enzyme activity. Each presentation is followed by a discussion.

A review of recent ideas of intracellular structure and the implications therein for metabolic regulation is given, with an explanation of why the nucleus may be considered an extracellular particle. The convincing argument that adenosine diphosphate is the most effective drug for respiratory control is brilliantly presented. The paper on control points in phosphorylating respiration is an outstanding contribution to the mechanism of oxidative phosphorylation. The Pasteur effect (inhibition of fermentation by respiration) is defined and explained as clearly as it probably ever can be. One of the discussions, on digital computer analysis of interaction of glycolysis and respiration, demonstrates important metabolic regulations which are susceptible to experimental test. In the concluding discussion, the idea of feedback control of enzymatic processes is given in detail. The various and complicated attempts to define feedback all come back to its original engineering concept: the control of input by output.

This conference was attended by 31 outstanding biochemists, of whom 10% were Nobel laureates. To biochemists, this book is thus a brilliant and important report. To anyone interested in the chemistry of cellular growth and how to influence it, this book is indispensable. To research-minded medical men it should be most informative. To the general practitioner, reading this book would probably involve more input than would be gained in output.

Cole & Elman Textbook of Surgery. By Warren H. Cole, M.D., Professor and Head of Department of Surgery, University of Illinois College of Medicine, Chicago. With 49 contributing authors and consultants. Foreword by Evarts A. Graham. Seventh edition. Cloth. $17. Pp. 1224, with 1000 illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1959.

This new edition of a well-recognized and widely used textbook of surgery has been extensively rewritten and modernized. Its preface acknowledges the contributions of Dr. Robert Elman and regrets that his death occurred before the book could be published. It also contains a foreword by the late Dr. Evarts A. Graham. Dr. Cole has arranged this excellent revision with the aid of 49 competent contributors. Nine new chapters and 297 new illustrations have been added. This edition affords the reader a broad coverage of the field of surgery. The volume begins with an excellent chapter on the history of surgery, progresses through methods of examination and the general categories of surgery, and ends with a chapter on medical ethics and conduct. It is well adapted to the needs of the medical student. At the same time it provides valuable reading and reference material for physicians during internship and afterward. This textbook can be highly recommended.

QUESTIONS AND ANSWERS

TUBERCULIN TESTING

To the Editor:—*Although it is a well-known fact that the intradermal tuberculin test is more reliable than the patch test, I should like to know the present consensus as to the best method of tuberculin testing in mass surveys, such as in school children.* *M.D., New Jersey.*

Answer.—Although the values of the tuberculin test were soundly established early in this century, there are probably few if any tests with which so many persons have dabbled with reference to the kind of material, dosage, methods of administration, reading procedures, and specificity of various degrees of reaction. A considerable number have had their names attached to some phase of the tuberculin test. There is no doubt that all of this work has been done in good faith in endeavors to improve materials, methods of administration, and interpretation. However, in a few instances overenthusiasm in efforts to make the test do more than it is capable of accomplishing has resulted in erroneous deductions and confusion.

In testing, tuberculin has been administered subcutaneously, epidermally, percutaneously, and intracutaneously. Some have even instilled it into the nose, urethra, vagina, and rectum. Solutions of various strengths, ointments, jellies, etc., have been devised and used. The subcutaneous administration first practiced by Robert Koch was sometimes harmful because of the large dose employed. Therefore, Clemens von Pirquet devised a harmless epidermal scratch test, which he began to use in 1903. Administration consisted of applying tuberculin to a superficial scarification in the skin. It was this method with which Anton Ghon made his classic postmortem study and concluded that the tuberculin test is specific for the presence of tuberculous lesions. This is a good method of administering tuberculin. In 1928, Stewart devised a method which consisted of placing a drop of tuberculin on the skin and making a needle puncture through it into the skin. This resulted in reactions equal to those produced by the scarification method. This method was revived by Heaf in 1951, who produced an instrument for making multiple punctures in the skin. This is also a good method.

In 1908, Lautier moistened a pledget of absorbent cotton with 1% solution of tuberculin. This was bandaged to a cleansed area on the surface of the skin. The same year, Moro made a pomade consisting of equal parts of tuberculin and lanolin which he rubbed into cleansed skin. Lautier's method was revived by Vollmer and Goldberger under the name of patch test in 1937. In 1929, Lovet reported an extensive study of the percutaneous method which revealed that it is as satisfactory as the scarification method of Pirquet.

In 1908, Mantoux introduced the intracutaneous method of administration. The main advantage claimed was that a measured amount of tuberculin could be injected into the layers of the skin with no possibility of it being removed by clothing, etc. Accuracy with reference to amount may have been overestimated because of human error in administration, as well as the possibility of some solution being lost by leaking back through the needle track. This method made possible rough determination of degree of sensitivity of tissues to tuberculoprotein. It has been employed approximately 400 million times by veterinarians in testing cattle in the United States. They adopted it in 1920 and have found no reason to change. In 1926, Stewart and Collins made a careful comparison of the scarification method of Pirquet and the intracutaneous method of Mantoux on school children and reported that "a certain small percentage of children may have a positive Mantoux test in spite of the fact that the Pirquet is negative."

Each method of administration has had its proponents and opponents. This also applies to dosage, methods of reading, etc. The epidermal method of Pirquet, the percutaneous method of Moro and Lautier leading to the patch test, and the intracutaneous method of Mantoux are all good tests for diagnostic and epidemiologic work among persons with a high degree of sensitivity to tuberculoprotein. In such tissues, it is only necessary to introduce tuberculin into cleansed pores of the skin. It makes little difference whether it is rubbed into the pores or applied over the opening of the pores on a patch. A reaction will be elicited. This is also true when tuberculin is applied to a superficial skin scarification, enters through superficial punctures in the skin, or is injected into the layers of the skin. Thus, any of these methods is satisfactory when a high degree of allergy exists. This usually applies to children and young adults in whom allergy has been acquired so recently that it is still on a high plateau. After an invasion of tubercle bacilli occurs, allergy gradually develops, reaching a level detectable by the characteristic tuberculin reaction within three to seven weeks. Before it reaches this high degree, a larger dose than usual may detect its presence. Again, after

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

the lesions of the primary complexes are well encapsulated, if reinfections do not occur, allergy begins to wane and may reach such low levels that larger doses of tuberculin than usual are necessary for its elicitation. Thus, for a few weeks while allergy is developing and for long periods while it is waning, the percutaneous, the scratch, and the puncture methods may not be adequate, making larger doses by the intracutaneous method necessary.

Several studies have compared reactions of the skin of the same person to various methods. There is considerable evidence that the patch test is equal to 0.1 mg. of tuberculin administered intracutaneously. Probably the majority of persons in the United States who use the tuberculin test extensively prefer the intracutaneous method of administration. It can be highly recommended. However, situations and circumstances exist where, for one reason or another, the intracutaneous method cannot or will not be employed. Under such conditions, enthusiasm for "perfection" (there is no perfect method) should not condemn the use of a method "slightly below par" with the result that all help is lost.

CHRONIC DRAINING SINUS

To the Editor:—*A patient had an abdominoperineal resection for carcinoma of the rectum, and a complete hysterectomy was done at the same time. The colostomy has functioned properly during the year since the operation, but the perineal wound has not healed. In spite of treatment a sinus persists. Have you any recommendations? What treatment can one give after injection of opaque medium along the sinus tract and delineation of the tract on a roentgenogram?*

Stanley E. Peterson, M.D., Brockton, Mass.

Answer.—It would be of interest to know the treatment that was used initially. The first step is to obtain a scout roentgenogram of the pelvis for identification of a possible foreign body. Then injection of an opaque substance and radiography should be done to determine the size and extent of the sinus tract or cavity. Opinions about treatment differ; the choice is between tolerance of the sinus tract, by the patient, if the symptoms are minimal, and its complete excision, which can involve extensive dissection—much more than preliminary roentgenographic studies might suggest.

CHEMOTHERAPY OF GASTRIC CANCER

To the Editor:—*What is the efficacy of chemical cytostatic agents in the treatment of a patient with stomach cancer? What drugs are available?*

Mario Russo, M. D., Naples, Italy.

Answer.—Unfortunately, none of the anticancer agents are very effective in the treatment of solid tumors, including carcinoma of the stomach. A few regressions of several months' duration have been reported in such patients with the use of nitrogen mustard and thio-TEPA. During the past year experiments have indicated that 5-fluorouracil may be more effective than the older compounds. A new compound, 5-FUDR, has been synthesized, which may be better than 5-fluorouracil. These two drugs are fairly toxic, however, and must be given cautiously. Although subjective improvement may take place in 20 to 40% of patients receiving them, improvement lasts for only a few months.

MORGUE REFRIGERATION TEMPERATURE

To the Editor:—*What is the necessary temperature for a morgue refrigerator? The bodies are not usually in the refrigerator for more than 12 to 18 hours, but occasionally they are kept several days before embalming.* *M.D., Illinois.*

Answer.—In mortuary refrigeration the temperature must be high enough so that the surface of a stored body is not frozen but sufficiently low to inhibit bacterial and autolytic processes. Temperatures between 35 and 40 F (2 to 5 C) afford good preservation for purposes of both histopathological examination and embalming. There is a 2 or 3 F "lag" in controlling thermostats and it is recommended that these not be set below 34 to 35 F, to prevent freezing.

MALNUTRITION AND ACHLORHYDRIA

To the Editor:—*Can gastric achlorhydria be a sequel of extreme and prolonged malnutrition, as was the experience of a patient who was a prisoner of war for five years?*

G. L. Jackson, M.D., Cleveland.

Answer.—Gastric achlorhydria resulting from malnutrition or debilitation is usually temporary, for the parietal cells are resistant to extreme trauma. About 18% of the American population has achlorhydria. The incidence of achlorhydria developing spontaneously increases with the age groups, and studies have reported an incidence as high as 33% in persons over the age of 65 years. Because of the relatively high incidence of spontaneous achlorhydria one could assume that in this instance the achlorhydria is not related to starvation.

SPHINCTER OF ODDI

To the Editor:—*Does the sphincter of Oddi normally allow regurgitation of duodenal contents into the bile duct? Roentgenograms of a patient revealed barium in the common bile duct, which was thought to indicate a fistula, but on subsequent investigation no abnormality was found.*

Ward A. Shaver, M.D., Fergus Falls, Mo.

Answer.—Regurgitation from the duodenum to the common duct occurs frequently. When a T-tube is placed in the common duct, there may be excessive loss of duodenal secretions (via tube drainage), with impairment of electrolyte and water balance.

Incompetence of the sphincter of Oddi must take place in these cases. Professor Mallet-Guy of Lyon, France, has made an extensive study of the sphincter of Oddi in patients with various types of biliary tract disease. His publications may be consulted for additional information.

ACHONDROPLASIA AND HEREDITY

To the Editor:—*An achondroplastic dwarf wonders whether or not she will have abdormal children. She will have to be delivered by cesarean section because of cephalic-pelvic disproportion. She is one of four siblings, two of whom are also dwarfs. Her mother is a dwarf, and her grandmother is of short stature. Her husband is normal and has no family history of dwarfism. Should she be sterilized after delivery?*

D. J. Rothenberger, M.D., Mentone, Calif.

Answer.—Achondroplasia is inherited as a dominant trait in this family. This is the usual mode of inheritance for this condition, so there is a 50% probability that any child born to the patient will be an achondroplastic dwarf. A decision about sterilization must take into consideration not only the probability of abnormal children, but also the necessity of repeated cesarean sections if the patient will not use effective birth-control measures.

CHEMICAL CAUTERY OF THE CERVIX

To the Editor:—*When is chemical cautery of the cervix indicated?* *M.D., Minnesota.*

Answer.—During the past several years the indications for cauterization of the cervix, chemical or otherwise, have become fewer and fewer. When any type of malignancy is suspected cauterization of any kind is contraindicated, since it makes the histological diagnosis difficult or impossible because of tissue destruction. For treatment of patients with common cervicitis proper hygiene and antibiotic medicaments applied locally are most efficacious. Cervicitis rarely requires conization of the cervix.

SEQUELAE OF GASTRECTOMY

To the Editor:—*Please itemize sequelae that can occur months or years after a subtotal gastrectomy.*

W. M. Fowlkes Jr., M.D., Wendell, N. C.

Answer.—These sequelae include marginal, or jejunal, ulceration; peristomal gastritis (with possible gross hemorrhage); peptic esophagitis or peptic ulcer of the esophagus; the dumping syndrome, with excessive weight loss; intestinal malabsorption, diarrhea, deficiency pattern, and tetany; carcinoma of the fundus of the residual stomach; intestinal obstruction from postoperative adhesions; jejunogastric intussusception; anemia: secondary anemia or possible macrocytic anemia after extensive or total resection of the stomach; and possible gastroileostomy (misplaced anastomosis).

BODY CHEMISTRY AFTER DEATH

To the Editor:—*The inquirer on "Body Chemistry After Death" in* The Journal, *June 20, 1959, page 1009, may be referred to a similar comment on "Postmortem Blood Sugar" (Naumann, H. N.:* J. A. M. A. 157:780 *[Feb. 26] 1955). The following comments may be helpful.*

Chemical studies on body fluids from bodies refrigerated for about 10 hours after death (Hamilton-Paterson, J. L., and Johnson, E. W. M.: J. Path. & Bact. 50:*473 [May] 1940; Hill, E. V.:* Arch. Path. 32:*452 [Sept.] 1941; Naumann, H. N.:* Arch. Path. 47:*70 [Jan.] 1949, and* Am. J. Clin. Path. 20:*314 [April] 1950; Tonge, J. I., and Wannan, J. S.:* M. J. Australia 1:*439 [April 2] 1949) have shown major postmortem biochemical changes to be a decrease in glucose content by glycolysis (except in vena cava and right heart blood in which high glucose concentrations may be derived from liver glycogenolysis), and unexplained rise in urea content, an increase in potassium content by diffusion through more permeable cell membranes, an increase in phosphorus content by esterase activity, and a decrease in carbon dioxide content due to liberation of organic acid radicals, e. g., lactic acid (Naumann, H. N.:* Proc. Soc. Exper. Biol. & Med. 98:*16 [May] 1958). Minor postmortem biochemical changes include a moderate increase in bilirubin and cholesterol and slight decrease in sodium, chlorine, and protein contents, while calcium levels remain unchanged (Naumann, H. N.:* Am. J. Clin. Path. 26:*495 [May] 1956).*

These postmortem chemical changes are mainly in or near cells or cellular tissues and thus are greater in blood than in cerebrospinal fluid and in the latter more than in the vitreous body of the eye. The smallest change is in urine. Postmortem chemical analysis of cerebrospinal fluid and vitreous body, which may be done under certain conditions even after embalming, will indicate the antemortem blood constituents better than other specimens (A. M. A. Arch. Ophth. 62:356 *[Sept.] 1959).*

In spite of extensive biochemical changes that have taken place 10 hours after death it has been possible to establish postmortem averages, ranges, and criteria for interpretation of values beyond these ranges (except for potassium values even shortly after death), allowing a limited diagnostic conclusion as to the conditions of the body at the time of death.

Hans N. Naumann, M.D.
Kennedy Veterans Administration
Medical Teaching Hospital
Memphis 15, Tenn.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*It should be stressed that chemical studies done on postmortem specimens allow "limited diagnostic conclusions."*

WASHINGTON NEWS

Drug Company Investigation . .
Stilbestrol-Treated Chickens Barred . .
Unsaturated Fats Advertising . .

FIRST PHASE OF DRUG HEARINGS CONCLUDED

The Senate antitrust subcommittee charted further hearings on the drug industry after a week-long session in December, questioning three major producers of drugs for the treatment of arthritis and related ailments.

Subcommittee Chairman Estes Kefauver (D., Tenn.) indicated he would call officials of companies specializing in antibiotics when the hearings resume in mid-January. Producers of insulin, tranquilizers, and sulfonamides were slated to testify later. Kefauver said he expected eventually to hear from spokesmen of all the 15 largest drug makers.

After the first week of sessions at which officers of Merck & Co., Inc., The Upjohn Company, and Schering Corporation, testified, Kefauver contended that the evidence "clearly shows" that prices are excessive. He said legislation might be needed.

Company officials countered that the senator was distorting profit figures and not taking into account the high cost of research and distribution in the industry.

John T. Connor, Merck president, said the drug industry is "highly competitive." In the first three years after cortisone was introduced, Merck slashed the price 90%, he said, and other producers were forced to lower prices similarly to remain competitive. This similarity of pricing represented competition, not lack of it, he told the subcommittee.

Questioned about issuing licenses to permit other companies to manufacture patented ethical drugs, Connor said that companies that invest in research to produce new drugs are entitled to get back their investment and make a profit.

Dr. E. Gifford Upjohn, president of The Upjohn Company, said the industry is unique in that prices are coming down in a period of general inflation. Replying to Kefauver's criticism of the role of the "detail" men in giving physicians a firsthand rundown on company products, Upjohn said two-thirds of all physicians regard the detail men as their most important source of product information.

Seymour N. Blackman, executive secretary of Premo Pharmaceutical Laboratories, Inc., of South Hackensack, N. J., said the industry is overcharging the public by 750 million dollars a year, a figure which he said represented expenditures for advertising and promotion. He labeled such programs "brainwashing" of physicians.

Sen. Alexander Wiley (R., Wis.) disputed this charge and said he thought physicians were capable of exercising their own expert judgment on what drugs to prescribe.

In a New York speech, Dr. Austin Smith, president of the Pharmaceutical Manufacturers Association, said the drug industry has become a whipping boy for persons who are seeking socialized medicine.

"How much would people really be helped if drug prices were reduced by an amount equivalent to the net profit margin for the pharmaceutical industry? Such pennies will not pay for gas, light, rent, food, clothing, or medical care in general. Isn't it time all of us tried to get things in proper perspective instead of looking for whipping boys?" he asked.

TREATED CHICKENS WITHDRAWN FROM MARKET

The government and the poultry industry agreed to a voluntary plan to halt sales of chickens treated with a synthetic sex hormone known to cause cancer in experimental animals. Less than 1% of all chickens were affected.

Arthur S. Flemming, Secretary of Health, Education, and Welfare, said housewives would be able to buy chickens with confidence after the action.

Representatives of the poultry industry and food retailers agreed to discontinue sales of treated birds immediately. And manufacturers of the hormone, stilbestrol, immediately suspended sales of the product for use in poultry.

Flemming said the treated poultry withdrawn from sale will be purchased by the Department of Agriculture.

Stilbestrol is also widely used in the production of beef cattle, sheep, and lamb, but Flemming said, "No residues of the chemical have been found in beef, mutton, or lamb."

Later, the HEW secretary said the incident pointed up the need for dropping the "grandfather" clause from the food and drug law to allow HEW to "automatically revoke" all outstanding approvals for use of possibly harmful substances. At present,

(Continued on next page)

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References: 1. Ellison, R. R. and Burchenal, J. H.: J. Chronic Dis. 6:421 (Oct.) 1957. 2. Ultmann, J. E., Hyman, G. A., and Gellhorn, A.: J.A.M.A. 162:178 (Sept. 15) 1956. 3. Bethell, F. H.: J. Chronic Dis. 6:403 (Oct.) 1957.

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HEW can only bar use in new applications but cannot order previously allowed usage discontinued.

Charles B. Shuman, president of the American Farm Bureau Federation, attacked Flemming's recommendation, and said he would seek an amendment requiring HEW to prove in court that seized foodstuffs contain harmful substances.

Flemming had declared that while scientists study the possible dangers of some chemical additives for food, "The consumer should not, in effect, be asked to serve as a guinea pig."

"It is important to bear in mind that the use of stilbestrol for agricultural purposes has no bearing whatsoever on the use of this drug in the practice of medicine," said Dr. Roy Hertz of the National Cancer Institute. "Medical use of stilbestrol was first authorized in 1941. The drug can only be sold on a physician's prescription and therefore is administered only under medical supervision.

"It is generally agreed among physicians that drugs of this type are quite useful in the control of the symptoms of many patients without significant hazard under the usual conditions of clinical practice," he said.

"UNSATURATED FATS" CLAIMS HIT

The Food and Drug Administration urged the public not to believe claims that use of certain treated salad oils, shortenings, or oleomargarine will prevent heart attacks or strokes.

Health claims by some sellers of "unsaturated fats and oils" violate federal misbranding laws, FDA said.

"Addition of unsaturated fats and oils to the otherwise unchanged ordinary diet will not reduce blood cholesterol [levels] and prevent heart attacks and strokes," the agency claimed.

"The role of cholesterol in heart and artery diseases has not been established," said FDA. "A causal relationship between blood cholesterol levels and these diseases has not been proved. The advisability of making extensive changes in the nature of the dietary fat intake of the people of this country has not been demonstrated."

"There is widespread interest in the possible relationship between blood cholesterol levels and heart and artery diseases," said FDA Commissioner George P. Larrick. "As a result, reference to the term 'cholesterol' in the labeling of common foods now being offered to the public may have the effect of a claim of special value for preventing or treating these diseases.

"Scientific investigations of fatty substances as a possible factor in lowering blood cholesterol [levels] and preventing heart disease should be continued, and this policy statement does not interfere in any way with legitimate research and clinical evaluation of unsaturated fats in the diet," he said. "It is our responsibility, however, to point out that the public has been misled into relying prematurely on data which are still experimental, incomplete, and contradictory and to head off false and misleading promotions based on such data."

FDA pointed out that nutrition scientists believe it is impracticable for a person to add enough unsaturated fats to an otherwise unchanged diet to bring about any significant change in blood cholesterol content. Increased weight, they add, is the only result that is likely to be achieved by increasing the intake of fats.

MISCELLANY

The National Institutes of Health has made 71 grants totaling $1,751,270 for research in various aspects of aging. The grants have gone to investigators in 21 states and the District of Columbia. Twenty-seven of the grants, amounting to $536,942, are continuations of previous projects, while 44, totaling $1,214,328, are new grants. The grants are part of a continuing NIH program of study into the health-related characteristics of the aging process.

A Public Health Service brochure stresses the importance of prompt diagnosis of little strokes and indicates that early treatment often avoids other more serious strokes. "Little Strokes—Hope Through Research" tells the story of stroke patients who have survived their attack to live long, useful lives. It urges careful diagnosis, proper treatment and rehabilitation, and an intelligent attitude by family and patient. Single free copies may be obtained from the National Institute of Neurological Diseases and Blindness, Bethesda 14, Md.

Four research grants for studies in the improvement of hospital services and facilities were announced by the U. S. Public Health Service. The Johns Hopkins Hospital, Baltimore, will receive $66,771 for a two-year analysis of patterns of demand for hospital services. The University of Maryland Hospital in Baltimore will receive $1,984 for an exploratory study of the feasibility of automation in hospitals. Western Reserve University, Cleveland, will receive $25,000 for a study of the outpatient department and the attitudes of patients who come there toward the services available. The Georgia Department of Public Health, Atlanta, will receive $6,950 for a study of the lighting needs of intensive-care units in hospitals.

The Food and Drug Administration announced that three new products for removing wax from the ears are causing painful injuries and are being voluntarily withdrawn from the market. They are Kerid, Cerulav, and Cerumenex. The FDA said some sensitive users have suffered swelling and soreness of the ears from the products.

About 87 million Americans have now had at least one shot of polio vaccine, and 68 million have had three or more injections, according to a Public Health Service study. Among persons under 40 years of age who are most vulnerable to the disease, more than 34 million, or almost 30%, have had no vaccine, the PHS reported. Among children under 5 years of age, the group that accounted for 43% of the paralytic cases this year, 4,500,000 have had no vaccine.

Plans for a new advertising campaign to be conducted by the Advertising Council and sponsored by PHS, the American Medical Association, and National Foundation were announced. To be launched in the spring, it will urge support for local vaccination drives.

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Facilities for complete and frequent blood counts must be available for patients receiving 'Leukeran', 'Myleran' or 'Purinethol'.

Full information about these products will be sent on request.

References: 1. Unugur, A., Schulman, E., and Dameshek, W.: New England J. Med. 256:727 (Apr. 18) 1957. 2. Burchenal, J. H., Karnofsky, D. A., Murphy, M. L., Ellison, R. R., Sykes, M. P., Tan, C. T. C., Mermann, A. C., Yuceoglu, M., and Rhoads, C. P.: Am. J. M. Sc. 228:371 (Oct.) 1954. 3. Altman, S. J., Haut, A., Cartwright, G. E., and Wintrobe, M. M.: Cancer 9:512 (May-June) 1956.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.

1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

December

American Association for the Advancement of Science, Morrison Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. of Virginia, Richmond, Va., Director of Public Information.

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Mid-Winter Clinical Convention for Ophthalmologists and Otolaryngologists (29th), Research Study Club, Ambassador Hotel, Los Angeles, Jan. 17-22. Dr. Norman Jesberg, 500 S. Lucas Ave., Los Angeles 17, Secretary-Treasurer.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc.. Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

Arizona Academy of General Practitioners and Arizona Psychiatric Association Psychiatric Seminar, Phoenix, Ariz., Feb. 13-14. Dr. James L. Grobe, 5630 N. 27th Ave., Phoenix, Ariz., Chairman.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Clinical Congress of Abdominal Surgeons, Deauville Hotel, Miami Beach, Fla., Feb. 1-5. For information write: Clinical Congress of Abdominal Surgeons, 633 Main St., Melrose 76, Mass.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Memphis, Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memphis 5, Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago, Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-Treasurer.

American Academy of General Practice, Philadelphia, Mar. 18-24. Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, Mo., Executive Director.

American Association for the History of Medicine, Inc., Charleston, S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Institution, Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broadmoor, Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Portland Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, New Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ. of Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. 30. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Treasurer.

American Laryngological Association, Deauville Hotel, Miami Beach, Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of Technology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Society, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Fla., Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minneapolis 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deauville Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, Montreal, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, N. Y., Executive Assistant.

American Radium Society, Caribe Hilton Hotel, San Juan, Puerto Rico, Mar. 17-19. Dr. Robert L. Brown, Robert Winship Clinic, Emory University, Atlanta 22, Ga., Secretary.

Missouri State Medical Association, Sheraton-Jefferson Hotel, St. Louis, Mar. 13-16. Mr. T. R. O'Brien, 634 N. Grand Blvd., St. Louis 3, Executive Secretary.

National Health Council, National Health Forum, Miami, Fla., Mar. 13-18. Mr. Philip E. Ryan, 1790 Broadway, New York 19, Executive Director.

National Multiple Sclerosis Society, New York City, Mar. 8. Mr. Donald Vail, 257 Fourth Ave., New York 10, Secretary.

Neurosurgical Society of America, Del Monte Lodge, Calif., Mar. 30-Apr. 2. Dr. Raymond K. Thompson, 803 Cathedral St., Baltimore 1, Secretary.

New Orleans Graduate Medical Assembly, Roosevelt Hotel, New Orleans, Mar. 7-10. Miss Irma B. Sherwood, 1430 Tulane Ave., New Orleans 12, Executive Secretary.

Southeastern Surgical Congress, Roosevelt Hotel, New Orleans, Mar. 21-24. Dr. B. T. Beasley, 1032 Hurt Bldg., Atlanta 3, Ga., Executive Secretary.

Southwestern Surgical Congress, Riviera Hotel, Las Vegas, Nev., Mar. 28-31. Miss Mary O'Leary, 1213 Medical Arts Bldg., Oklahoma City, Okla., Executive Secretary.

April

Alabama, Medical Association of the State of, Admiral Semmes Hotel, Mobile, Apr. 21-23. Mr. W. A. Dozier Jr., 19 S. Jackson St., Montgomery 4, Executive Secretary.

American Academy of Neurology, Eden Roc Hotel, Miami, Fla., Apr. 25-30. Mrs. J. C. McKinley, 4307 E. 50th St., Minneapolis 17, Executive Secretary.

American Association of Anatomists, Statler-Hilton, New York City, Apr. 11-16. Dr. Louis B. Flexner, Dept. of Anatomy, School of Medicine, Univ. of Pa., Philadelphia 4, Secretary-Treasurer.

American Association of Immunologists, Chicago, Apr. 11-15. Dr. Calderon Howe, Columbia Univ. College of Physicians and Surgeons, New York 22, Secretary-Treasurer.

American Association of Pathologists and Bacteriologists, Hotel Peabody, Memphis, Tenn., Apr. 28-30. Dr. Russell L. Holman, Dept. of Pathology, L. S. U. School of Medicine, New Orleans, La., Secretary.

American Association of Railway Surgeons, Drake Hotel, Chicago, Apr. 7-9. Mr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Executive Secretary.

American College of Obstetricians and Gynecologists, Netherland Hilton Hotel, Cincinnati, Apr. 2-6. Mr. Donald F. Richardson, 79 W. Monroe St., Chicago 3, Executive Secretary.

American College of Physicians, Mark Hopkins & Fairmont, San Francisco, Apr. 4-9. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

American College of Surgeons, Sectional Meeting, Hotel Leamington, Minneapolis, Apr. 11-13. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Kahler Hotel, Rochester, Minn., Apr. 14. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Dermatological Association, Inc., Boca Raton Hotel, Boca Raton, Fla., Apr. 8-12. Dr. Wiley M. Sams, 308 Ingraham Bldg., Miami 32, Fla., Secretary.

American Physiological Society, Chicago, Apr. 11-15. Ray G. Daggs, D.Sc., 9650 Wisconsin Ave., Washington 14, D. C., Executive Secretary.

(Continued on page 30)

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DIAGNOSIS AND TREATMENT OF OSTEOPOROSIS

James A. Nicholas, M.D.
and
Philip D. Wilson, M.D., New York

Among 105 patients hospitalized for spontaneous vertebral compression fractures, there were 55 (9 men and 46 women) in whom the diagnosis of osteoporosis was accepted after the exclusion of all other known causes of such fractures. Back pain was the chief symptom listed by all patients, but it was not always concurrent with the fracture. A history of cholecystectomy, hysterectomy, and a diet low in calcium content was common to one-third of the women. The condition was not limited to postmenopausal patients. No biochemical or roentgenographic evidence of benefit was noted in any of the patients receiving hormone therapy, but more than half said they felt better while taking hormones. Bed rest with gradual return to normal activity was adequate treatment in many cases, but about one-third of the patients required absolute bed rest for six weeks. Ten patients failed to improve and went on to a series of relapses and hospitalizations.

OSTEOPOROSIS is a disease which produces a quantitative decrease, but not qualitative histological change, in bone. The effects of this disease are among the chief contributory causes of a variety of fractures and subsequent crippling deformities. In the older population especially this disease is one of the important causes of long-term illness, with its concomitant pain, suffering, and prohibitive expense.

Although there are 800 or more cases of osteoporosis reported in the literature,[1] there are few which have had comprehensive long-term follow-up reported by orthopedic surgeons. This paper reports the characteristic features of 55 additional patients with osteoporosis, their treatment, and follow-up data on them.

In a recent study[2] of 105 patients admitted to the Hospital for Special Surgery between 1950 and 1958 with spontaneous vertebral compression fractures, we found a variety of diseases other than osteoporosis which produced rarefaction of bone with severe pain requiring hospitalization (table 1). Osteoporosis was a diagnosis arrived at only by careful exclusion of such conditions. Serum chemistry studies, direct bone biopsy, and marrow examination were repeatedly the most fruitful aids in differentiating other bone disorders from osteo-

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Assistant Professor of Surgery (Orthopedics), Cornell University Medical College (Dr. Nicholas), and Director of Research, Hospital for Special Surgery (Dr. Wilson).

Read before the Section on Orthopedic Surgery at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 11, 1959.

porosis. In another report[3] the authors noted that studies of 24-hour urine calcium excretion, with use of Knapp's formulation,[4] were also of value in establishing the differential diagnosis of rarefying bone disease.

TABLE 1.—*Established Diagnosis in 105 Patients with Spontaneous Vertebral Collapse*

Diagnosis	Patients, No.
Osteoporosis	55
Idiopathic osteoporosis	4
Postmenopausal and senile osteoporosis	51
Malignancy	25
Metastatic carcinoma	12
Multiple myeloma	9
Other	4
Hyperadrenalism, with rheumatoid arthritis	9
Osteomalacia (malabsorption)	6
Polycythemia vera	3
Hyperparathyroidism	2
Other	5

Analysis of Age, Sex, and Number of Vertebral Fractures

The 55 patients suffering from osteoporosis constituted more than half of the 105 patients admitted with spontaneous vertebral collapse to the hospital between 1950 and 1958. There were 9 men and 46 women who received the diagnosis of osteoporosis. The age incidence of this group of patients is depicted in table 2. Data from 57 other patients who had adequate trauma or known malignancy with fractures were discarded from this study. Spontaneous vertebral compression was a prerequisite for the roentgenologic diagnosis of osteoporosis, although other criteria such as "increased vertical trabecular systems," "pencil cortices," and "codfishing" were usually present.

After exacting examination only 5 of 27 patients under the age of 55 years were given a diagnosis of osteoporosis. Of 78 patients over the age of 55 years, 50 were found to have osteoporosis.

Although most patients with osteoporosis in this series were between 55 and 75 years of age, the youngest patient was a man, 38 years of age, who had four vertebral compression fractures. Three marrow studies performed on him as well as two direct biopsies gave negative results. Repeated examination was completely unremarkable and the patient was diagnosed as suffering from idiopathic osteoporosis. One woman aged 44 (whose repeated examination gave a negative result) had severe osteoporosis, with six vertebral bodies fractured. Her history revealed that her menopause was induced by hysterectomy and oophorectomy for endometriosis at 29 years of age. There were three other patients with osteoporosis under 55 years of age, all women, two of whom were aged 49 and one of whom was aged 52 years.

It was also observed that, when the number of vertebral bodies fractured in a given patient was counted, there was usually a significant difference between the number of collapsed vertebrae in patients with osteoporosis and those in patients with primary or secondary malignant bone disease. Thus, of 16 patients in whom a diagnosis of bone malignancy was established after examination, 14 had no more than two vertebrae fractured. Only 10 of 55 patients with osteoporosis had one or two vertebrae fractured. Metabolic bone disease, osteomalacia, and osteoporosis were usually characterized by a multiplicity in the number of vertebral bodies fractured, whereas malignancy, with the exception of multiple myeloma, tended to produce one or two vertebral fractures. Of nine patients with multiple myeloma two had 10 or more collapsed vertebrae; three patients had one vertebral collapse; and the other four patients had between 3 and 6 collapsed vertebrae.

Other Locales of Fractures.—Six patients each had three or more other skeletal fractures after the age of 50 years. One patient had broken both wrists, one hip, and two humeral heads in the past In some, however, there were no other fractures Since spontaneous fractures are rare in long bones unless they are due to malignancy or osteomalacia other sites of fracture were not used as a criterion in this study.

Other Case Data

Duration of Symptoms.—The nature and occurrence of symptoms varied. Pain was often acute sometimes chronic or exacerbating, and at times absent. All of the patients, however, were admitted with acute, severe back pain and spasm. Of the 55 patients 47 had had backache of intermittent degree and intensity for some time prior to their present hospitalization; in 8 it had been for only one week prior to admission, 16 had had backache for from one week to six months, 4 for six months to one year, 21 for one to five years, and 6 for over five years.

In the younger patients, backache was more apt to be of sudden onset, without any prior history. In general, the older the patient, the longer the history of backache. Indeed, one patient complained of having had back pain for 30 years and insisted that, at the time of admission for new collapse, the pain was of the same type and in the same region as it had been throughout the years, except that it was of greater intensity. Three patients had intermittent backache of over 20 years' duration, and in these patients there were multiple vertebral fractures. However, none of the obvious old collapsed vertebral bodies apparently produced pain of sufficient intensity to warrant hospitalization until the present episode. Although there was no

TABLE 2.—*Age Incidence of Fifty-five Patients with Osteoporosis*

Age, Yr.	Patients, No.
36-45	2
46-55	3
56-65	32
66-75	13
Over 75	5

significant relationship noted between the onset of clinically discernible osteoporosis and the first appearance of backache, eight patients had their first history of back pain associated with a fresh vertebral collapse. In general, it can be said that the cause of pain in such patients is often obscure. Pain is present without evidence of further collapse and may be due to microfractures, but this is difficult to prove.

Relation of the Menopause to Disease.—There were 46 women in this series. Their menstrual history is shown in table 3.

One patient had primary amenorrhea, with severe multiple compression fractures. Three other women whose periods were still present had considerable osteoporosis. One must assume, therefore, that in these patients, in whom no other cause for this striking demineralization could be found, the osteoporosis should not be labeled the postmenopausal variety. However, in this series, 21 women had periods which terminated prior to the age of 45 years. In most, clinical symptoms suggesting the onset of the menopause were found by the age of 40 years. Eight women had cessation of menses prior to the age of 40, six by hysterectomy or oophorectomy.

TABLE 3.—*Age at Cessation of Menses of Forty-six Women with Osteoporosis*

Age, Yr.	Patients, No.	Menopause Induced by Hysterectomy or Oophorectomy
Never had a period	1	...
Still present	3	...
Under 35	4	3
36-40	4	3
41-45	13	4
46-50	9	3
51-55	10	1
Over 55	2	...
Total	46	14

Since there were nine men in this series, as well as three premenopausal women and one woman who had never had periods, it can be seen that over 20% of the patients had osteoporosis which could not be related to changes associated with the menopause. This should furnish ample evidence for the obscure pathogenesis of this disease and emphasize the fallacy of ascribing it solely to the menopause.

Relationship of Gastrointestinal Disease and Calcium Intake in Patients with Osteoporosis.—Our dietitians determined the average calcium intake of the patients at the time they were admitted. It was estimated that 18 patients had an average of less than 500 mg. of calcium intake per day—a low figure, which was explained by the fact that none of these patients drank any milk. Twenty-two patients had an average intake of between 500 and 800 mg. of calcium a day, and 15 patients had an average of over 800 mg. of calcium intake per day.

The patients were questioned and examined for the presence of gastrointestinal tract disease. Of the 46 women, 22 had a history of biliary tract or gastrointestinal disease which required medical treatment prior to admission. Of the nine men, one had a history of previous ulcer. These patients, however, did not have any evidence of osteomalacia.

Of interest was the fact that twelve women who had had prior cholecystectomy had also undergone hysterectomy. Only one of these women had an average calcium intake exceeding 700 mg. a day. Perhaps a reason for accelerated net calcium loss was that most patients had cut down their milk intake because of fatty food intolerance. Thus, 25% of the women in this series had low calcium intake, had had induced menopause, and had had cholecystectomy.

Marrow, Biopsy, and Laboratory Data.—Thirty-four marrow examinations were performed on 26 patients with osteoporosis. All gave negative results. Direct bone biopsy of lytic lesions, with 11 negative results, was done in 9 patients with osteoporosis. In the over-all series of 105 patients, there were 13 positive results of marrow examinations in 48 patients. One realizes, then, that this is an integral part of a complete examination and is especially helpful in the diagnosis of conditions which may be mistaken for osteoporosis. In the osteoporotic patients no unusual laboratory values were found, with the exception of transient hypercalcemia in a patient in whom repeat studies gave normal results.

Treatment

Management of Back Pain and Fractures.—Treatment of osteoporotic patients was directed to the management of their compressed vertebrae during the acute and convalescent phases, and the long-term efforts were directed to reducing the possibilities of a negative mineral balance.

Plaster of paris casts were not used in this series except in two patients in whom attempts were made to reduce the fracture. Otherwise, compression was accepted but the spine was kept from flexing by not allowing the patient to sit up for two to four or more weeks. On hospitalization, with acute pain, the patients were sedated and kept on strict bed rest as long as was necessary to relieve pain. Some were kept on oscillating beds, but this had no visible effect on the patients' convalescence. Table 4 shows the number of days of strict bed rest these patients required in the hospital prior to their discharge.

Of 55 patients 20 required bed rest for more than four weeks, and 18 were hospitalized for six or more weeks. It was apparent that, in many cases, allowing the patient to sit up, to walk, or to go to the bathroom too soon exacerbated the symptoms. Such setbacks were frequent and troublesome and associated with the minutest of strains.

Supports and Physical Therapy: In two patients body spicas were used for three months; 28 patients were fitted with corsets; and 25 patients had various types of braces provided for them when they were allowed to walk. A few of the patients noted that they felt the need for intermittent use of supports for up to six or seven years, but in most cases supports were discarded in six months. Careful fitting usually rendered supports, at first uncomfortable, symptomatically helpful.

Diathermy and other forms of heat therapy, although frequently used, did not seem to play any role in accelerating symptomatic recovery. In some cases heat was definitely thought to increase pain. Occasionally, warm, moist packs were of symptomatic value in the early phase of treatment.

Complications: Severe exacerbations occurred in 12 of the 55 patients within six months, requiring their readmission. A number of complications occurred, in addition to the deformity which resulted from increased shortening. The significant complications included cystitis (eight patients), vomiting secondary to ileus (seven patients, one of whom died), renal calculi (two patients), pneumonia (two patients), thrombophlebitis (two patients), decubitus ulcer (two patients), and pulmonary embolus (one patient).

Table 4.—*Amounts of Time Spent on Bed Rest and in Hospital of Fifty-five Patients with Osteoporosis*

Time, Wk.	Strict Bed Rest, Patients	In Hospital, Patients
Up to 1	1	0
1-2	7	8
2-3	15	10
3-4	12	5
4-5	8	14
5-6	8	10
6-7	0	4
7-8	2	2
Over 12	1	1
Over 16	1	1

The most important complication to recognize early was paralytic ileus, with severe electrolyte imbalance. It was necessary to perform gastric lavage in four patients with severe ileus associated with back pain and fracture.

Follow-up Examinations: In this series 25 patients returned to their usual way of life. They were classified as comfortable up to four years after discharge. In the other 30 patients, pain continued to be a troublesome problem. However, 20 of these were able to carry on with useful activity but with the need for rest. Of the remaining 10 patients with severe symptoms, 4 had surgical explorations in an almost desperate attempt to alleviate severe back pain. Six others continued to complain bitterly and seek medical attention.

Fifteen patients required two hospital admissions, six patients required three admissions, and three required four admissions; the last three were still in pain at the time of last follow-up examination.

Suggested Program for Management of Acute Phase: In an effort to reduce exacerbations, the following regimen is suggested. After the first three weeks, if pain has subsided, the patient should not be allowed to be up, even without symptoms, for more than one-half hour at a time. This program should be insisted on for a week or two. After this, gradual lengthening of periods of activity, but with insistence on one or more daily rest periods, will give a good result. After a month exercises are begun, including the use of heel cord stretching, abdominal and gluteal setting, and those designed to increase breathing capacity. Later, if provision for swimming or pool therapy at regular intervals can be provided, considerable improvement in strength may be expected.

Injections for Tendinitis: One of the common sources of pain in patients with round back due to osteoporosis results from stretching of the ligaments over the spinous processes, usually at the apical part of the curve of the round back. Indeed, in some patients, once they were ambulant tendinitis was the sole cause of persistent back pain. In such cases the instillation of a local anesthetic preparation such as procaine and 25 mg. of hydrocortisone was sometimes quite effective. In order to determine this, it is helpful to examine the patients while they lie prone over a table so that the palpating finger can precisely localize the site of pain. If it is sharply localized to one fingertip-sized area over a spinous process or rib, local injection treatment is indicated. We have the impression that in some of the patients who complained the vertebral compression was not in itself painful but, rather, the pain was due to tendon or ligamentous irritation. In such instances, the patient's response to injection treatment was as dramatic as it occasionally is when tendinitis occurs elsewhere in the body.

Follow-up in Convalescence: The patient's height, weight, respiratory excursions, and mobility should be checked periodically, even when the patient is asymptomatic. The patient should be repeatedly instructed on proper habits of bending and lifting and should be told that the disease is a lifelong one requiring long follow-up care. An active program of life, interspersed with adequate, frequent, but short periods of recumbent rest is the *sine qua non* in persons afflicted with severe osteoporosis.

In a certain number of patients, osteoporosis and its sequelae constitute a chronic, refractory, disabling illness and lead to a vicious cycle of enforced recumbency, continuing fractures, depressions, and discouragement. Nevertheless, most patients can be expected to improve, despite roentgenograms which may give the appearance of extreme deformity and demineralization. Improvement often requires months to years, and considerable time should be spent with the patient to prevent discouragement and consequent failure to abide by the outlined programs of treatment.

The Use of Hormones.—Thirty-eight patients received some hormone therapy; 17 discontinued this therapy within a few months and 21 received hormone therapy continuously for one or more years. These included one patient who received such therapy for one year, three who received it for two years, five for three years, four for four years, three for five years, three for six years, one for seven years, and one for eight years. Although almost half of the patients discontinued hormone therapy because of disinclination or significant side-effects, more than half of the patients were able to continue therapy with hormones. Indeed, 13 patients at the time of writing have taken hormones continuously for four or more years (table 5). Of the 21 patients receiving therapy with hormones for a year or more, 2 were men and 19 were women.

Preparations in Use: A variety of preparations have been used. Since estradiol benzoate has been one of the few preparations[5] with the documented ability to produce calcium retention in balance studies, it was used, in doses varying from 1.66 to 3.32 mg., several times weekly. Methyltestosterone, 10 to 20 mg. per day, was also added as a starting regimen. Three patients have continued to receive such therapy for six years without serious side-effects. On the other hand, most of the patients could not continue on such a program, unless dosages were reduced drastically, so other preparations have been used in such instances. Three patients have been given methyltestosterone, 10 to 20 mg. daily, and conjugated equine estrogens, 1.25 mg. a day, for at least five years with minor intolerance. Yet other patients have not been able to tolerate these same dosages for more than one month. As other preparations have become available, we have not been reluctant to use them. Among the preparations which have been used in patients in this series, with satisfactory results, from the standpoint of tolerance, are a preparation of 2.5 mg. of estradiol monobenzoate and 50 mg. of testosterone isobutyrate (Femandren linguets); one of estradiol and methyltestosterone in a 1:10 combination (Gynetone); one of 90 mg. of testosterone enanthate and 4 mg. of estradiol valerate (Deladumone); fluoxymesterone (Halotestin); conjugated equine estrogens (Premarin); one of 50 mg. of testosterone cyclopentylpropionate, 2 mg. of estradiol 17-cyclopentylpropionate, and 5 mg. of chlorbutanol, in cottonseed oil (Depotestadiol); and a multivitamin preparation with estrogens and d-desoxy-ephedrine hydrochloride (Mediatric). We have had no experience with the use of strontium.

TABLE 5.—*Follow-up Data on Patients with Osteoporosis*

Year Admitted	Patients, No.	Progress Followed to Present	Deaths	Hormones Used Continuously	Hormones Discontinued	Improved or Comfortable	Worse
1950-1951	4	3	1	1	2	3	0
1951-1952	4	4	0	3	1	4	0
1952-1953	8	6	0	5	3	6	2
1953-1954	11	8	0	4	3	9	2
1954-1955	12	10	1	3	2	9	2
1955-1956	6	6	0	3	3	5	1
1956-1957	8	6	0	1	2	5	8
1957-1958	2	2	0	1	1	2	0
	55	45	2	21	17	43	10

The problem of optimum dosage is a confusing one. We have had great difficulty in raising doses to so-called metabolically active levels, since intolerance has followed rapidly. Moreover, it has not been convincingly shown that increased dosages mean increased net storage of calcium. It seems to us more important to use the greatest quantity the patient can be counted on to take, over as long a period of time as possible, with minimum intolerance, of whatever preparation one is most familiar with.

Complications: We have not been able to use hormones with confidence, however, since patient tolerance has varied immensely. The usual policy has been to use smaller rather than larger doses, and to use mixed therapy. Of 21 patients receiving hormones for one or more years, bleeding has occurred at one time or another in one-third of the women. Hirsutism has been frequent. Fluid retention has not been bothersome, with two exceptions. The complications, although at times troublesome, have been minimized, provided the patient has been completely briefed about the problems prior to the start of treatment.

No cases of cancer have occurred, nor are we impressed that the often-quoted relationship between the use of sex hormones and the production of cancer is actually substantiated by any valid clinical evidence in human beings. Unfortunately, the measure of effectiveness of hormone treatment is purely a subjective one.

Other Results of Hormone Treatment: The useful effect of hormones in most of these patients has been seen in the response of the patient's mood. Such changes have included increased appetite, ability to sleep better, less preoccupation with troubles, and greater capacity for activity. Patients who desired to continue treatment felt that they experienced a definite boost with hormone treatment, which was not noted when hormone administration was discontinued. No biochemical evidence of benefit was noted, nor was there any increased roentgenographic density noted, even in patients receiving long-term treatment. However, the beneficial effect of hormone therapy has been impressive enough often enough to warrant its use in patients with more severe cases of osteoporosis, despite the problems of intolerance.

The use of hormones depends on some knowledge of their action. In some patients it is possible to counteract excessive estrogenic or androgenic effects by "juggling" the mixed dosages and by cyclic administration and "rest" periods. If the patient has been told that bleeding may occur and if she is carefully checked for this by a gynecologist, one can sometimes continue therapy indefinitely and eventually reach a program of dosage with a preparation which is well tolerated. In cases of intolerance, various preparations should be tried. We have found that it is usually possible to find some dose of some estrogen-androgen hormonal combination which is tolerable.

Indications for Diagnostic Examination and Treatment

It is our feeling that if the patient is under 55 years of age, and especially if there are only one or two vertebrae spontaneously compressed, every diagnostic test should be utilized to rule out some condition other than osteoporosis, including open biopsy, marrow examination, and 24-hour urine calcium determination with the patient on fixed as well as unrestricted diet. Serum calcium, phosphorus, alkaline phosphatase, and total serum protein levels and electrophoresis of plasma protein should be obtained in such patients. Roentgenography of the skull as well as intravenous pyelography should be performed. Usually, the diagnosis can be established by such means, if a condition other than osteoporosis exists. Where indicated, consultations to evaluate the gastrointestinal and renal systems are helpful.

In the event that all test results are negative, one can assume that osteoporosis is the diagnosis. However, especially with patients in the younger age group, some unusual condition such as rheumatoid arthritis of the spine (Marie-Strümpell arthritis), osteitis deformans (Paget's disease), or polycythemia vera may eventually be diagnosed as the cause of collapse. Therefore, patients with the diagnosis of "idiopathic" osteoporosis who are under the age of 55 years should be rechecked in a year or more, with repeat study.

Once the diagnosis has been satisfactorily established, it has been our policy to use hormone therapy only if the patient's history has been characterized by chronic, exacerbating attacks, with roentgenographic evidence of obvious demineralization. Patients who have had no previous history of back pain and who convalesce satisfactorily from their first hospitalization are not given hormone therapy unless exacerbation and readmission ensue.

In some patients, no matter how vigilant the treatment with all of the available techniques, improvement does not occur. We have the impression that patients who have had rheumatoid arthritis treated with corticosteroids or other concomitant illness are apt to do poorly. In such cases, months drag by and every attempt to render these patients ambulant is met by a setback. It is because of such pathetic problems that physicians should be alert to the needs for an early diagnosis of osteoporosis and for establishing a prompt and early program of future activity geared to the patient's abilities.

Summary and Conclusions

Osteoporosis is the most common of all diseases producing vertebral compression. The diagnosis can be made only by the exclusion of other causes. Osteoporosis is characterized by remissions and exacerbations, producing shortening of stature, pain, and deformity. In this series of 55 patients, more than one-half had symptoms lasting for one to five or more years. In this series, 12 of the 46 women afflicted with severe osteoporosis had a history of low dietary calcium intake, induced menopause, and cholecystectomy. Such a triad should alert one to the possibility of the presence of this disease.

Relapses are common. Of 55 patients in this series 10 did not improve. They required a series of successive, seemingly never-ending, hospitalizations and continual care. On the other hand, most patients with severe osteoporosis can be returned to a reasonably comfortable life, especially if they are taught to adapt themselves to their functional abilities. One-third of these patients required absolute bed rest for six weeks before symptoms subsided sufficiently for ambulation. It is not necessary to treat the fractures with plaster casts. Indications for hormonal treatment are guided largely by the duration and severity of the patient's symptoms and by their tolerance to sex hormones. Long-term hormone therapy was tolerated by about half of the patients in whom it was used.

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PHYSICAL MEDICINE IN MANAGEMENT OF PATIENTS WITH POSTMASTECTOMY LYMPHEDEMA

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Lymphedema affecting the upper extremity after radical operations on the breast was studied in 220 patients. Limb volumes measured by displacement of water made it possible to assess the results of treatment. The treatment program here described consisted of a period of some days in a department of physical medicine and rehabilitation, followed by a period of home treatment which was usually prolonged. During the first period manual and mechanical massage were used, in addition to isometric exercises and spiral bandaging. During the second period the patient carried out certain instructions, especially involving exercise, bandaging, and elevation of the extremity. The results were sometimes only palliative, but the objective data as well as the reactions of the patients show that this program generally reduced the discomfort and disability caused by the lymphedema.

One of the most distressing sequelae of radical mastectomy is the development of lymphedema of the upper extremity. Haagensen[1] stated that it is "the only postoperative complication of any consequence." If the edema is mild, the distress may be related only to the appearance of the extremity and the problem of fitting the sleeves of clothing to it. When the edema is moderate or severe, it may also produce distress because the limb is cumbersome, because of sensory disturbances, including pain, or because of the patient's high susceptibility to cellulitis after minor trauma or insect bites. If it is severe, the patient may be almost completely disabled.

In 1948, Stewart and Treves[2] reported lymphangiosarcoma occurring as a late complication of postmastectomy lymphedema. It may develop after the edema has persisted for eight or more years. It has been suggested that the incidence may run as high as 10% in those patients with postmastectomy lymphedema who survive long enough.[3] Whether minimizing the severity of the lymphedema affects this incidence is not known.

Incidence and Causes of Postmastectomy Lymphedema

Reports on the incidence of postmastectomy lymphedema vary widely. Some of this variability is due to differences in the definition of edema. There are no volumetric studies of the incidence of lymphedema in a large series of patients having radical mastectomies. Further confusion is created by mixing together what Haagensen[1] called "postoperative edema," which occurs in the immediate postoperative period and is due to "some sort of fault in surgical technique," and "secondary edema."

The literature on the subject seems to deal with at least three syndromes. One of these is an acute transient edema occurring immediately postoperatively. The second is an acute painful edema with its onset in the first three or four weeks after operation. This has been reported to respond favorably to a variety of therapeutic agents and procedures, including adrenal corticosteroids, phenylbutazone, antibiotics, and sympathetic blocks. It also seems to be transient. The third syndrome, with which this paper is primarily concerned, is characterized by persistent but usually painless edema several weeks, months, or even years, after operation. While the precise incidence of this syndrome is not known, it is likely that it occurs to some degree in about 50%, and is a significant complication in 10 to 15%, of patients undergoing radical mastectomies of the Halsted type.

Etiology.—Disagreement exists about whether the condition is due primarily to venous or to lymphatic obstruction and on the role played by the autonomic nervous system. Villasor and Lewison[4] and Treves[5] concluded that there was no single cause. Treves[5] has made the following statement.

> Probably the most frequent cause is interference with the return of lymph because of ablation of the profunda lymphatics with the nodes of the axilla. Interference may be due directly to the axillary dissection or to cicatrization following infection or fibrosis following roentgen-ray therapy. Angulation of the vein, interfering with both venous return and return of lymph from vessels in the wall of the vein, and reflex spasm of the axillary vein must likewise be assessed as bearing directly on the problem.

In Treves' series of 319 patients, obesity was a predisposing factor. The extent to which the axillary nodes were involved by metastasis at the time of operation was not related to the incidence or severity of the edema. Postoperative infection or delayed wound healing, acting alone, was not associated with an increased incidence of edema.

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When superimposed on other factors, however, these augmented the incidence and severity of the swelling.

Haagensen[1] agreed with Halsted's[6] early concept that postmastectomy lymphedema is due to infection occurring in an arm with an impaired lymphatic circulation, even though this infection may not readily be detected. He described the work of Ju and Habif, which showed that there is delayed lymphatic drainage from the arm for the first two to four weeks after operation. Although drainage approaches normal at the end of a month, it never reaches normal. In addition to this, the precipitating cause of the edema, Haagensen stated, is infection, and he adds, "if the infection is treated early the process is reversible." Both Haagensen and Treves pointed out the constant threat of lymphedema that faces most postmastectomy patients. Treves[5] has made the following comment.

> It is well to remember that the onset of swelling in patients previously free from this complication may be initiated by any minor infection or trauma. Friction from clothing, trauma to the arm, a scratch or a mosquito bite, sunburn or a minor thermal injury, paronychia or ringworm of the nail, a cut at the time of manicure, any of these may induce lymphedema, which often persists. The circulatory balance is so fine that seemingly trivial incidents may produce this distressing complication; and, once produced, the process is rarely reversible.

Surgical Treatment

Modifications of the Halsted operation to provide a lymph-draining bridge across the axilla have been tried, with varying degrees of success, in patients suffering from postmastectomy lymphedema. Other modifications have involved resection of the axillary vein or artery. The literature on this problem has been extensively reviewed by Treves.[7] Surgical correction, once lymphedema has occurred, has been based on resection of the lymphedematous tissue or attempts to stimulate the formation of new lymphatic channels to bridge the axillary obstruction. Drainage with Southey tubes and blocking of the stellate ganglion have also been described. Amputation has been performed in rare cases.

Nonsurgical Treatment

The nonsurgical treatment of patients with postmastectomy lymphedema is based, first, on elevation, massage, and use of the muscular pumping action to increase lymphatic and venous flow out of the limb, and, second, on elastic support of the limb to keep the swelling from recurring. Such measures are often palliative, in the sense that the elastic support cannot be abandoned. However, in a significant but as yet undetermined proportion of cases, elastic support can be left off without a return of the swelling.

Physiological Considerations.—The rationale of such nonsurgical management is based principally on Starling's hypothesis about the factors affecting the passage of water through the capillary wall. As Drinker and Yoffey[8] pointed out, this is now more an established mechanism than a hypothesis. Figure 1 is a diagram incorporating the principal features of the Starling hypothesis as well as some of the concepts put forth by Pappenheimer.[9]

Pappenheimer pointed out that the capillary wall is about 0.3 μ thick. The pores which are presumed to be in the intercellular cement substance make up only about 0.2% of the surface area of the capillary wall. Through the pores small molecules such as water and electrolytes can pass easily. The water passes through the pores partly because of filtration pressure, and the substances dissolved in it wash through the pores with the water; however, most of the transfer of water and its solutes through the pores is by diffusion, which occurs readily because the distance through the wall is so small. There is some restriction to diffusion imposed by the size of the pores and this exerts a "sieving" action, particularly on the larger molecules. Oxygen, carbon dioxide, and lipid-soluble substances pass through the wall anywhere and have a large surface area available for their transfer. Since the protein molecules cannot pass freely through the pores, they exert an osmotic pressure, which draws water into the capillary from the tissue fluids. As the filtration flow of water through the pores decreases, the sieving effect is less marked and the proteins of the plasma and tissue fluids come more into equilibrium. Such a reduction of filtration would occur if the hydrostatic pressure of the tissue fluids increased toward the level of the capillary hydrostatic pressure, as in firm or tense edema.

Protein that leaves the blood circulation through the capillary wall returns to the blood, if at all, by way of the lymphatics.[10] The excess of water entering the tissue spaces through the capillary wall over that reentering the capillary also leaves by way of the lymphatics.

The difference between the osmotic pressure due to plasma colloids and that due to tissue-fluid colloids is the effective osmotic pressure tending to draw water into the capillary from the tissue fluids. It is theoretically a trifle greater at the middle of the capillary than at either end. The difference between the plasma hydrostatic pressure and the tissue hydrostatic pressure is the effective hydrostatic pressure which tends to drive water out of the capillary. Because of the decrease of blood pressure, the effective hydrostatic pressure falls progressively as the blood passes from the arteriolar to the venous end of the capillary.

The relationship between these two effective pressures is shown in figure 2. Wherever the effective hydrostatic pressure is greater than the effective osmotic pressure, more water leaves the capillary than enters it. Wherever the effective hydrostatic pressure is less than the effective osmotic pressure, more water enters the capillary than leaves it. Anything that increases the effective hydrostatic pressure or decreases the effective osmotic pressure will disturb the balance in favor of the passage of more water out of the capillary and less back into it. If the lymphatics do not take care of the excess, the accumulating water will build up the tissue hydrostatic pressure until an equilibrium is reached again.

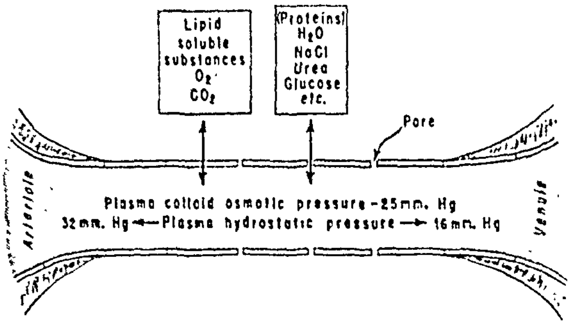
Lipid
soluble
substances
O_2
CO_2
(Proteins)
H_2O
NaCl
Urea
Glucose
etc.
Pore
Arteriole
Venule
Plasma colloid osmotic pressure -25mm. Hg
32mm. Hg ← Plasma hydrostatic pressure → 16mm. Hg

Fig. 1.—Factors influencing exchange of water between capillary blood and tissue fluid. Protein molecules can pass through pores only with difficulty. Values for different pressures are arbitrary but of order of magnitude of those that actually exist—tissue hydrostatic pressure, 8 mm. Hg; tissue colloid osmotic pressure, 10 mm. Hg.

Microcirculatory observations have shown that there is much variation from moment to moment in the flow of blood through individual capillaries in a capillary bed.[11] This would imply considerable change in the hydrostatic pressure within the capillary. While the Starling hypothesis may not be applicable at all times to any individual capillary, clinical experience with the production and correction of edema due to various causes supports the idea that the hypothesis does apply to capillary beds as a whole.

The capillary hydrostatic pressure may be increased by arteriolar dilatation (produced by local heating, generalized heating, or muscular activity) or by venous obstruction (produced by such factors as inactivity of the muscle "pump," congestive heart failure, constricting clothing, and incompetence of the valves). The tissue hydrostatic pressure may be reduced by stretching of the skin and subcutaneous tissues, with loss of their elasticity. These tissues, then, are abnormally loose when the excess fluid is removed and the swelling can easily recur. The osmotic pressure due to plasma colloids may be reduced by hemodilution, by specific decrease in the plasma proteins, or by increase in permeability to proteins of the capillary membrane. In the last-mentioned event, or in the event of a slowing of filtration rate and its accompanying reduction of the sieving of plasma proteins from the water leaving the capillary, the concentration of protein in the tissue fluids will increase.

All these factors are known to produce edema. So also may lymphatic obstruction produce edema. Lymphatic obstruction may result from inactivity of the muscle "pump," or incompetent valves in the dilated vessels, as well as from the more obvious factor of destruction by surgery of communicating channels between the superficial and deep lymphatic collecting systems.

On this theoretical basis one would expect lymphedema, once established, to tend to be a progressive condition which would not subside spontaneously. Furthermore, any nonsurgical program for its correction would have to provide for a "shoring up" of the tissue hydrostatic pressure while the return of elasticity of the skin and subcutaneous tissues toward normal is awaited.

Mayo Clinic Program.—The program of treatment[12] that my colleagues and I have employed for the past four years has aimed at reducing the volume of the extremity by simple standard procedures and at endeavoring to prevent by bandaging any swelling of the extremity for a sufficient period to permit shrinkage of the subcutaneous tissues and skin to a more nearly normal size, so that tissue turgor would then be maintained at this size. The treatment has been in two phases. The first is a period of treatment in the section of physical medicine and rehabilitation and the second a program of self-treatment at home. Since improvement may be slow and may require considerable attention for weeks or months, the financial burden may be excessive, if the patient is not taught to carry on her own treatment at home.

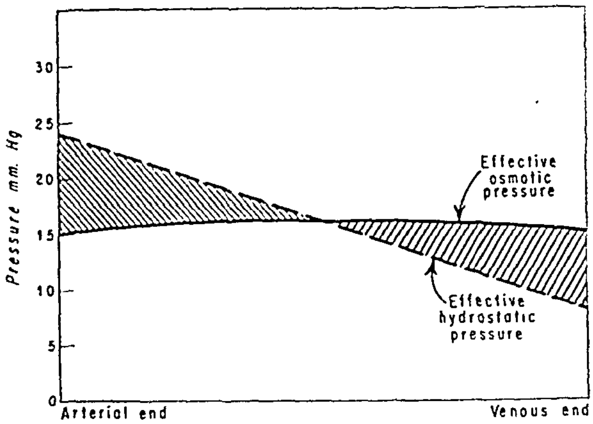

Fig. 2.—Relationship between effective hydrostatic pressure and effective colloidal osmotic pressure. Water passes through capillary wall in both directions throughout its length. Where effective hydrostatic pressure is greater than effective colloidal osmotic pressure, more water leaves capillary than enters it (*left*). When this relationship is reversed, net exchange of water is reversed (*right*).

The treatment in the section of physical medicine and rehabilitation has ideally been given twice daily. It has consisted of a 30-minute period of centripetal mechanical massage with use of a "vasopneumatic" device. This is followed by 7 to 10 minutes of manual kneading and stroking massage to reduce edema, particularly in the more indurated areas. The patient is instructed in the method of performing isometric or nearly isometric exercises of the arm and forearm muscles to use the pumping action of the muscles on the veins and lymphatics. She is taught how to bandage her own upper extremity with an adequate elastic bandage. We have used two 3-in. woven bandages stitched together end to end and applied from the dorsum of the hand up to about the level of the insertion of the deltoid muscle. A simple spiral bandaging technique seems to be as good as any. We have occasionally tried a figure-eight technique at the elbow, but it leads to constriction of the venous and lymphatic circulation at that level. There is no need to incorporate the fingers or the thumb in the bandage. The patient begins to practice the procedures of the home treatment program between treatments in the section so that she will know how to do them when she goes home.

TABLE 1.—*Measurements Before Treatment of 193 Patients with Lymphedema**

		Control Arm, Liters			
Edematous Arm, Liters	Total Patients	Less Than 1.5	1.5-1.9	2.0-2.4	2.5 or More
1.5-1.9	6	1	5	..	..
2.0-2.4	24	1	14	9	..
2.5-2.9	42	..	14	26	2
3.0-3.4	61	1	9	39	12
3.5-3.9	34	..	5	13	16
4.0-4.4	14	..	..	4	10
4.5-4.9	4	..	..	2	2
5.0-5.4	4	..	..	..	4
5.5-5.9	2	..	..	..	2
6.0 or more	2	..	..	1	1
Total	193	3	47	94	49

* All measurements made by water displacement.

The home program has been devised so that the patient can carry it out independently. It consists of elevation of the extremity, isometric exercises, and bandaging. The limb should be elevated most or all of each night on pillows or on some type of frame, if the patient prefers. The bandage is applied in the morning before the patient gets out of bed. When the tissues are loose and inelastic a great amount of swelling can pour through the capillaries into the tissues in 20 or 30 minutes, and for this reason it is important to apply the bandage prior to arising. During the day the patient takes a half-hour out of each two hours to lie down, with the arm elevated. She performs the isometric exercises frequently during this half-hour period. At the end of the half-hour she removes the bandage and reapplies it immediately. On retiring at night she may remove the bandage a few minutes before lying down, for purposes of bathing the limb. The bandage is not worn at night. The use of rubber household gloves will permit the patient to immerse her hand with the bandage on.

After two or more weeks on this home program, if the reduction of the swelling has been satisfactory, the interval between the periods of elevation, exercise, and changing of the bandage during the day is lengthened by an hour. Another increase can follow in another two or three weeks, if all goes well, and finally the patient should attend to her arm at about noon and before the evening meal, with additional rewrapping of the bandage should it become disarrayed. The speed with which the patient progresses with this program may be slower than that outlined above, particularly if the reduction in the edema is proceeding slowly. The objective is to get the arm as small as possible and keep it at that size while waiting for the tissues to shrink and regain their elasticity.

The patient is urged to avoid the use of local heat on the extremity, since heat is contraindicated in the presence of noninflammatory edema. Excessive use of the extremity must also be avoided, particularly in warm weather or in a warm room. Careless bandaging may obstruct the venous or lymphatic circulation and must be avoided, as should clothing with the same harmful feature.

It is not possible to determine in advance which patients will be able ultimately to go without elastic support. After the volume of the limb has been held at a minimum for about eight weeks, the patient tries leaving the bandage off in the evening for about two hours before bedtime. If the tape measure detects no increase in size, the bandage may be left off for three hours the next evening. Regular increases are made until she has found out how long she can leave the bandage off without exacerbation of the edema.

The actual value of the vasopneumatic device in the treatment program is not known. A few patients have done well without it, but the number we have treated without it is too small for reliable comparison. Any machine may be expected to provide a rather inefficient massage, with regard to emphasizing the areas most in need of massage; however, a machine does not fatigue and may make up in time of action for what it lacks in efficiency of application. Other pumping machines are available, but I have not yet had the opportunity to use any of them.

TABLE 2.—*Measurements Before and After Treatment in Ninety-five Patients*

			Control Arm, Liters		
Edematous Arm, Liters	Group*	Total Patients	1.5-1.9	2.0-2.4	2.5 or More
1.5-1.9	A	2	2	..	..
2.0-2.4	B	7	5	2	..
	A	11	7	4	..
2.5-2.9	B	19	8	11	..
	A	32	8	23	1
3.0-3.4	B	32	5	23	4
	A	28	3	18	7
3.5-3.9	B	22	2	11	9
	A	14	..	4	10
4.0-4.4	B	8	..	2	6
	A	4	..	..	4
4.5-4.9	B	3	..	1	2
	A	3	..	1	2
5.0 or more	B	4	..	..	4
	A	1	..	..	1
Total		95	20	50	25

* A: after and B: before treatment over a few days in the section of physical medicine and rehabilitation.

Results.—From October, 1955, until April, 1959, 220 patients were seen in the section of physical medicine and rehabilitation at the Mayo Clinic because of lymphedema of the upper extremity. A previous report[13] presented some observations on 96 of these, seen in the period October, 1955, to August, 1957. A similar statistical analysis was made on the 124 patients seen from August, 1957, to April, 1959, to check the validity of the figures obtained from the first 96 cases. Since the results were in general nearly the same with the second group as with the first, the entire series has been grouped together in this report. Limb volumes were measured by displacement of water, as previously described.[12]

Of the total 220 patients, 27 have been omitted from the study for a variety of causes. Twelve had had some treatment for lymphedema either by us or elsewhere before any measurements were taken; five had a treatment program different from that used generally in this series; four had not had mastectomies; three had inadequate measurements before treatment; one was a man; one had edema that developed acutely after an insect bite 10 months after mastectomy, and this edema was already subsiding spontaneously when the patient was first seen; and one had had surgical excision of some of the lymphedematous tissue.

The distribution of the 193 cases included in this study is shown in table 1. Here the volumes of the edematous arms are grouped in relation to the volumes of the contralateral (control) arms. The table shows that although most of the edematous upper extremities were about 1 liter larger than the normal contralateral extremity, there was wide variability in the severity of the edema in the patients sent to the section of physical medicine and rehabilitation for its treatment.

For 95 patients, measurements were taken before treatment and at the end of a few days of treatment twice daily in the section, as outlined above. Table 2 relates the distribution of the volumes of the edematous arms to those of the normal arms for these 95 patients before and after the series of treatments. It can be seen that the difference in the sizes of the arms is generally less after treatment than before, since in each vertical column the number of arms that are much larger than their controls decreases, while the number of arms that are slightly larger than their controls increases. The extent of reduction of the edema in individual cases is obscured in this form of tabulation.

TABLE 3.—*Percentage Reduction of Edema During Treatment in Section in Ninety-five Patients*

	Before Treatment			After Treatment		
Greater Than Control Arm, %	No.	%	Cumulative Percentage	No.	%	Cumulative Percentage
0-19	4	4	4	23	24	24
20-39	33	35	39	40	43	67
40-59	35	37	76	25	26	93
60-79	13	14	90	4	4	97
80-99	6	6	96	1	1	98
100 or more	4	4	100	2	2	100
Total	95	100	...	95	100	...

Table 3 expresses the amount of the edema (difference in volume of the two upper extremities) as a percentage of the volume of the normal upper extremity. The 95 patients are again tabulated according to the severity of the edema before and after treatment. The comparison of the columns headed "Cumulative percentage" is the most striking feature of this table. It is seen that only 39% of patients had edema that was less than 40% of the normal volume of the arm before treatment, while 67% fell into this group after treatment. After treatment the edema in 24% of patients was less than one-fifth the volume of the normal arm, while only 4% could be classified thus before treatment.

TABLE 4.—*Rate of Improvement During Treatment in Section in Ninety-five Patients*

	Day of Treatment						Total Patients	
Reduction of Edema, %	1	2	3	4	5	6 or More	No.	%
0-9	1	4	6	2	1	2	16	17
10-19	1	3	5	1	1	2	13	14
20-29	..	7	4	3	1	4	19	20
30-39	..	2	8	3	5	5	23	24
40-49	..	1	2	2	3	4	12	13
50-59	..	..	..	1	1	4	6	6
60 or more	..	1	2	1	1	1	6	6
Total, no.	2	18	27	13	13	22	95	..
Total, %	2	19	28	14	14	23	..	100

The rate of improvement during twice-daily treatment in the section of physical medicine and rehabilitation is tabulated in table 4. Here the "percentage reduction of edema" is the amount of reduction of the limb volume expressed as a percentage of the initial amount of edema. Despite the fact that there are 95 patients in the series, not many fall in any one group. For the 27 patients who had treatment for three days a wide range of reduction of edema is evident. It is obviously not possible to make a firm prediction in a particular case that 20 or 30% of the edema will be gone in three days. Table 4 shows a tendency for greater reduction of edema to be obtained with longer periods of treatment. It will be seen that 9 of the 48 patients who stayed for four or more days of treatment obtained less than 20% reduction in the edema, while 9 others had reduction of the swelling by 50% or more.

In order to preserve the statistical advantage of larger groups of patients, table 5 has been constructed. As an example, 75 patients stayed three or more days for treatment and of these 75 patients 48 stayed for four or more days. While 65% of those who stayed for four or more days had reduction of more than 30% of their edema, only 57% of those remaining three or more days reached this goal. There is generally a greater difference between "three or more days" and "four or more days" than between any other consecutive periods of time in this table. This table, based on data from 95 patients, confirms the suggestion gained previously from 43 patients that the optimal period of time for this initial treatment in a physical therapy department is four days. It should be pointed out that the results in table 5 with regard to those improved "more than 30%" are not as good as those found with the smaller series,[13] but results in the "more than 40%" group are distinctly better.

No concerted effort has been made to collect long-term follow-up data and observations of the results of the home treatment program. In some instances it is known to have been successful, while in others it has failed to reduce the edema further or even to maintain a reduction obtained in the department. A few patients have been able to forego use of an elastic support without recurrence of the edema. At the other end of the scale, a few require continuous elastic support while up and around. Most patients probably fall in an intermediate group; they wear elastic supports while doing housework but can leave the support off for a few hours, particularly for social events, without an apparent increase in the size of the arm.

TABLE 5.—*Rate of Improvement During Treatment in Section of Ninety-five Patients*

		Improved					
		More Than 20%		More Than 30%		More Than 40%	
Days of Treatment	Patients	No	%	No.	%	No.	%
1 or more	95	66	70	47	50	25	26
2 or more	93	66	71	47	51	25	27
3 or more	75	55	73	43	57	23	31
4 or more	48	39	81	31	65	19	40
5 or more	35	29	83	24	69	13	37
6 or more	22	18	82	14	64	9	41

While our observations on the home treatment program are meager and probably are not representative of the entire group, they merit brief discussion. A total of 21 patients had measurements before and after treatment in the section of physical medicine and rehabilitation and after a period of treatment at home. Of eight who had improved little in the section, five either got worse or improved very little at home, but the other three did well at home. The other 13 had obtained relatively good results under treatment in the section. Of these, seven did rather poorly on the home program, but the other six did well on the home program and four have been able to abandon elastic support.

An additional 10 patients came back to the clinic but were not reevaluated in the section of physical medicine and rehabilitation. Of these, five were said to show improvement with regard to the lymphedema and in the other five no mention was made of the state of the arm.

It would seem fair to guess that about one-half the patients do fairly well with the home program while the other half either have no success with it or abandon the program when they discover after two or three months that the edema can be controlled only as long as they continue the supportive bandaging. The patient then chooses whether to continue with the annoyance of elastic support or the annoyance of a swollen arm. What influence, if any, this choice has on the likelihood that lymphangiosarcoma will develop is not known.

Some of the patients who did poorly on the home treatment program had followed that program conscientiously. All of those who did well on the home program had followed it conscientiously except one patient with moderate edema who found that bandaging aggravated the edema of the hand.

The recent trend has been to urge patients to continue with bandaging for about two months after the extremity has reached a minimal size. This minimal size may not be reached, however, for two to six months after the beginning of treatment. The over-all program may consume more time than was originally thought. The timing of the program must be adjusted according to the progress of the individual patient.

Comment

Treatment programs for patients with postmastectomy lymphedema such as that described herein are sometimes only palliative. However, most patients have been well satisfied with the results of the program, even if they have not been able ultimately to go without elastic support for more than a few hours at a time. Success with other methods of correcting the condition would appear to be met in no greater proportion of patients. Prevention is preferable to any method of correction now available, but it is not yet practicable.

Since the treatment program involves attending to the arm several times daily for several months, it is important that the patient learn how to carry it on without aid. It is economically burdensome to attend a physical therapy department frequently over such a long period. Professional treatment once or twice a week is not likely to be helpful. If rapid improvement is to be obtained, it will be in the first 7 to 10 days of treatment. Thereafter improvement will generally be slow whether or not professional treatment is continued in conjunction with the home program.

Several patients who have had success with our integrated program had previously had failure with the use of elevation, massage, or bandaging alone. The entire program, including the regular use of the pumping action of the muscles on veins and lymphatics, is more effective than the individual components alone. I have had little or no success in reducing the edema of a small number of patients who were unable to contract the muscles of the extremity.

Unless there is some good indication for the use of heat, such as pain in the shoulder or cellulitis of the extremity, it should not be used. Heat increases the tendency to edema, and edema is not an indication for its application in any form. Furthermore, the cutaneous blood supply has often been impaired by heavy roentgen irradiation, and this also is a contraindication to the use of heat.

Comparison of the results obtained by the 52 new patients reported here with the results obtained by the 43 reported[13] previously shows that our experience with this method of treatment has been remarkably consistent over the past four years. Although one cannot predict reliably what will take place in a given patient, the results to be expected in a group of patients are quite well established for this program of treatment.

Messrs. R. P. Gage and David Sperling assisted in the statistical analysis of data presented in this report.

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URETHRITIS-CYSTITIS SYNDROME IN THE FEMALE

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Chronic or recurrent urethritis, with or without cystitis (urethritis-cystitis syndrome) occurs so frequently in women that both the patients and their physicians are likely to let the lesion escape adequate treatment. The proximity of the urinary opening to the vaginal and anal orifices allows constant exposure of the urethra to the mixed bacterial flora of the vaginal canal and rectum. The most common pathological lesion found in 2,450 women with this syndrome was a meatal stricture of the urethra. Complete cure was more often accomplished when a specific etiological diagnosis had been obtained by careful inspection of the urethral meatus, palpation of the urethral glands, and panendoscopic examination of the urethral lumen.

The management of the female patient who has experienced one or more attacks of cystitis is an important part of the "everyday" practice of urology. Many of these patients have been labeled "neurotic" because of failure to recognize the underlying pathology.

This communication deals with a study of our experiences in treating urethritis and cystitis in female patients seen during the past 15 years. During this period, a total of 2,450 female patients were seen for whom a diagnosis of "urethritis-cystitis syndrome" was made. During the past five years visits by female patients have averaged 3,380 per year. The incidence of urethritis in women is high, and many factors play a part in this common malady, which affects most women at some time or other during their lifetime.

The role of obstructions in producing urinary symptoms and infections is elementary in urology. What is often lost sight of is the fact that obstruc-

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tion need not be complete or even noticed as such by the patient in order to produce symptoms. The complex embryologic development of the urinary tract makes one wonder that anatomic defects causing partial obstruction do not occur more often. Another reason these lesions are so often overlooked is that there is a general notion that the absence of a prostate in the female eliminates the lower urinary tract insofar as obstructive lesions are concerned. This misconception on the part of so many physicians, including a goodly number of urologists, so greatly disturbed the late Dr. Alfred Folsom, a famous urologist, that about 25 years ago he wrote a treatise entitled "The Female Prostate" in which he emphasized the high incidence of vesical neck and urethral pathology in the female.

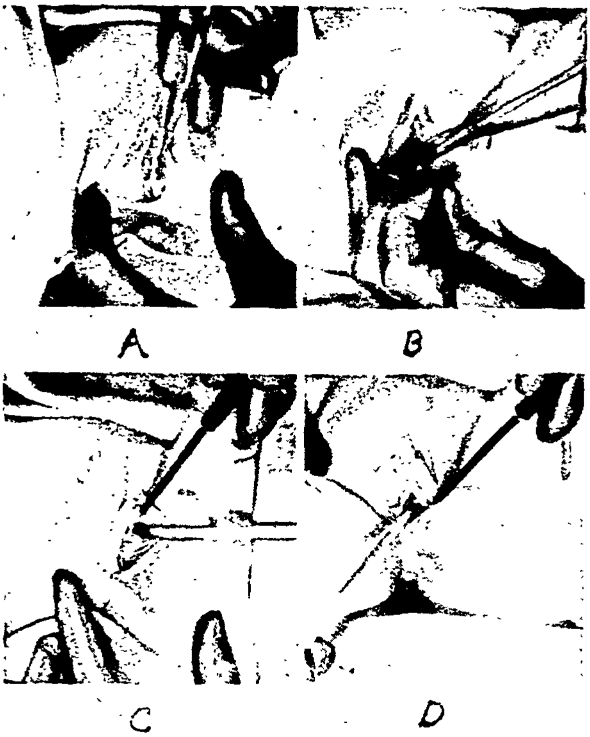

Fig. 1.—Meatotomy. *A*, incision in floor of urethra; *B*, excision of redundant lateral "flaps" of skin and mucosa; *C* and *D*, fulguration of margins of incision.

Symptoms

Even with a perfectly normal urethra and bladder, how is a woman to escape developing urethritis and recurrent cystitis in the face of repeated inoculations of pathogenic organisms due to the close proximity to the urethra of the vagina, the cervix, and the rectum? The anatomic changes that come about during the childbearing age further encourage lower urinary tract infections, and the changes resulting from the menopause also play important roles in the production of urethritis and recurrent cystitis.

Symptoms may be nonurinary in origin, as well as those referable to bladder and urethra. The urinary symptoms, in order of occurrence, are (1) frequency; (2) urgency; (3) dysuria; (4) nocturia; (5) straining to void; (6) slowness in emptying bladder; (7) dribbling; (8) retention of urine with residual; and (9) acute retention.

The nonurinary symptoms are (1) suprapubic soreness; (2) pain or soreness in flanks; (3) backache; (4) dyspareunia; (5) nervousness; (6) low-grade fever; (7) loss of appetite; and (8) nausea.

Most of these patients have multiple complaints, and many give a history of long-standing urinary symptoms. A great many women have urinary symptoms almost throughout life and seem to accept urinary frequency and occasional attacks of dysuria and urgency as more or less normal. Careful questioning often is necessary to bring out the true picture in most of these patients.

The pathology in the urethritis-cystitis syndrome is obstructive in nature in most patients. The narrow urethral meatus has been termed the most common anatomic defect in the urinary system. Obstruction that is caused by meatal stricture is the number one causative factor in urethritis and cystitis. A list of the abnormal findings is as follows: (1) narrow urethral meatus; (2) infected urethral glands; (3) urethral stricture; (4) hypertrophic urethritis; (5) vesical neck contraction; (6) trigonitis; (7) menopausal changes in urethral mucosa; and (8) urethral caruncle.

Extraurinary "associated" pathology is present in most patients in a variety of forms, such as (1) endocervicitis; (2) vaginitis and vulvitis; (3) anorectal area infection; (4) hemorrhoids; (5) cystocele; or (6) rectocele.

Diagnosis

Diagnosis of the urethritis-cystitis syndrome is made by correlation of a carefully taken history with the results of a proper examination. Result of urinalysis of a catheterized specimen is often normal, or nearly so, but in patients who are in a "flare-up" period the urine may contain numerous pus cells. The organisms found on urine culture vary considerably but most commonly are in the Escherichia coli group.

Careful inspection of the urethral meatus is important, and pressure over the urethra helps to determine the presence of infected urethral glands. When such pressure or stripping is applied, pus may be seen to exude from the urethral glands and the urethra is frequently quite sensitive to palpation. Calibration of the meatus and urethra should be a part of each examination and is better done by metallic Otis bougies à boule than by sounds. It is difficult to assess properly the meatus or the caliber of an urethral stricture by probing with a sound. A meatus of less than 26 French as calibrated by the Otis bougie à boule is classified as narrow and is usually subjected to meatotomy. This may be done as an office procedure, but it frequently is reserved to be done as part of the operative procedure when a transurethral resection of the bladder neck is done (fig. 1).

The panendoscopic inspection of the urethra is of the utmost importance in the diagnosis of urethritis and also in the determination of the degree of obstruction present in the vesical neck. There are some urologists who hesitate to diagnose vesical neck obstruction on the basis of panendoscopic findings. On the other hand, there are a great many urologists who have grown to depend on the panendoscopic picture for diagnosis of infravesical obstructions. We are among this latter group, and the results appear to justify this position. The bladder neck and trigone often may show hypertrophic changes, with intrusion of masses of thickened mucous membrane into the lumen of the posterior urethra and vesical neck. The roof of the urethra is the site of the most marked changes, and frequently the blood vessels in the mucosa are seen to be tortuous and dilated. The trigone and interureteric ridge often are thickened and hypertrophic, with a definite bas-fond behind the base of the trigone. Well-developed areas of bullous edema quite often are present in the vesical neck and trigone. The pathology most often encountered then is that of infected urethral glands, with or without a narrow meatus, and swollen and thickened mucous membrane with hypertrophic folds or polypoid masses in the posterior urethra and bladder neck. No other instrument discloses the pathological changes so well as the McCarthy panendoscope (fig. 2).

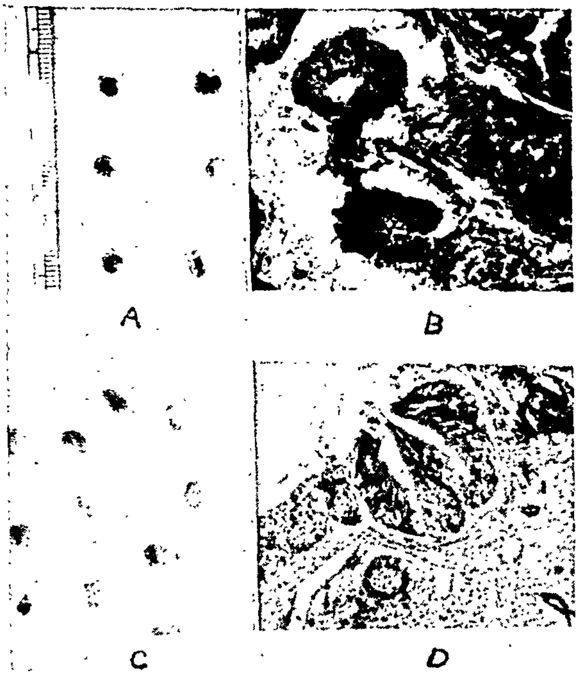

Fig. 2.—*A* and *C*, tissue resected from vesical neck; *B* and *D*, histological appearance of resected tissue revealing chronic inflammatory changes.

Treatment

Treatment is intended to clear up both the urethral and the "associated" extra-urinary pathology. About one-half of these patients may be treated satisfactorily as office patients. Meatotomy with excision of infected urethral glands is done, followed by urethral dilations at intervals of one to two weeks. Two points of technique of meatotomy in females that may be emphasized are as follows: 1. The incision is made with a no. 12 or "hawk bill" Bard Parker knife in the floor or "6 o'clock point" in the urethra. 2. Removal of each lateral flap of the opened meatus is then done in such a way as to excise most, if not all, of the infected urethral glands which are located in the anterior urethra. Excision of this mucosa effectively removes these glands. The bleeding is controlled satisfactorily by means of ferric subsulfate (Monsel's) solution.

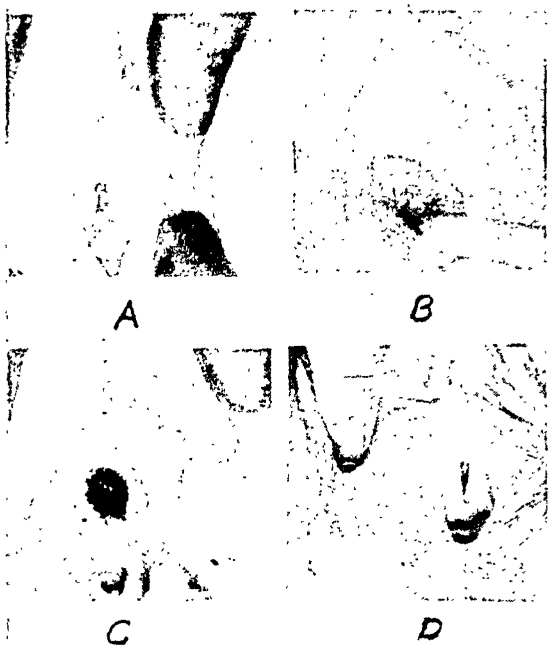

Fig. 3.—*A*, inflamed external meatus; *B*, traction on balloon bag catheter used to expose anterior urethra; *C*, appearance after fulguration; *D*, healed appearance six months later.

In addition to the meatotomy, electrofulguration of the anterior urethral mucosa is done when the urethritis is extensive or a caruncle or caruncle-like area exists. Exposure of this portion of the anterior urethra, and especially the area involved in a caruncle, is greatly facilitated by traction on a balloon bag catheter placed in the bladder (fig. 3).

Urethral dilations may be done with use of ordinary urethral sounds. However, about 20 years ago female sounds were devised by the late Dr. Harold Turner of Houston, Texas, and we prefer this type of sound. Dilations are carried up to 30 to 32 F, gradually. Each sound is left in place for about 10 minutes, and afterwards a freshly made mild silver protein (5% Argyrol) solution is injected or an antiseptic suppository placed in the urethra. Too rapid dilation is avoided. The size of the dilator is increased not more than one size on each successive treatment. Appropriate urinary antiseptics or antibacterial agents are prescribed in conjunction with the urethral treatments.

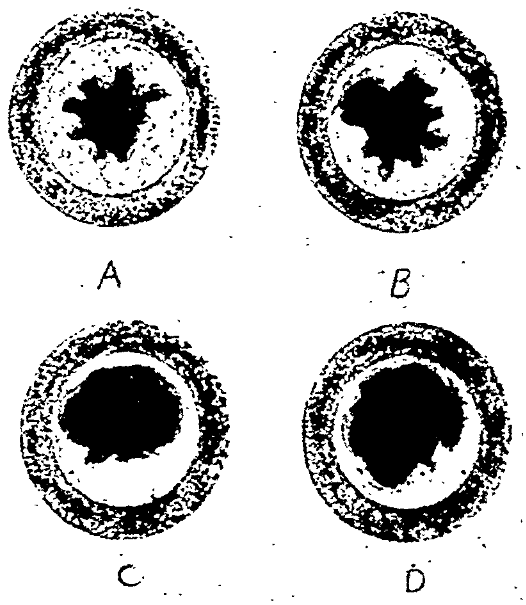

Fig. 4.—Cross-section drawings: *A*, cystoscopic appearance of vesical neck before transurethral resection; *B* and *C*, cystourethroscopic appearance of vesical neck during transurethral resection; *D*, appearance at completion of transurethral resection.

The cervix is inspected and proper measures carried out to eliminate endocervicitis as a focus of infection in the production of the urethritis. Cytological studies are done on all patients who have cervical erosion. In the elimination of simple endocervicitis it has been our practice to apply a 50% silver nitrate solution to the endocervix. Three to five such silver nitrate treatments at intervals of one to two weeks usually clear up the cervicitis. Warm saline or antiseptic douches are prescribed daily, and the patient is instructed as to the proper manner of administering the douche. We have been amazed at the large percentage of women who douche in an improper manner.

Patients who have a moderate to severe degree of obstruction or who have deep-seated infection in the urethral glands are advised to have a transurethral resection. This may be determined either on the basis of the severity of symptoms or on the panendoscopic appearance of the posterior urethra, vesical neck, trigone, and bladder. There may or may not be residual urine or bladder trabeculations (fig. 4).

We advise transurethral resection of the vesical neck and excision of urethral glands for about one-half of the women with recurrent urethritis-cystitis syndrome. The technique of transurethral resection is important and consists in careful resection of the hypertrophic or chronically inflamed mucosa of the proximal portion of the urethra. The mid-point of the urethra is considered to be the location of the sphincter, and extreme care is taken to limit the resection to the area proximal to this mid-point of the urethra. In following this technique we generally have had no incontinence, except in two patients who received either resection or fulguration past the mid-point in the urethra. Bladder neck and urethral suspension (Marshall-Marchetti) operation was effective in each instance in affording good urine control.

Transurethral resection of the female vesical neck is better begun in the roof of the urethra, followed by resection of the lateral walls of the vesical neck on either side. The floor of the vesical neck is resected last and care exercised not to cut too deeply on account of the danger of causing a vasicovaginal or urethrovaginal fistula. The final step in the operation is resection of the thickened trigone, particularly the portion between the ureteral orifices (fig. 5). This is comparable to excision of the wedge of tissue in the vesical neck when performing retropubic prostatectomy in the male. An indwelling balloon bag catheter, 22 French, is inserted, and the anterior urethral mucosa is exposed by traction on the catheter and fulgurated—a maneuver which is quite effective in eliminating the usually infected or inflamed anterior urethral mucosa, after which the meatus usually heals quite smoothly. Ordinarily the catheter is left in place for three days. The patient is dismissed from the hospital on the fifth or sixth postoperative day.

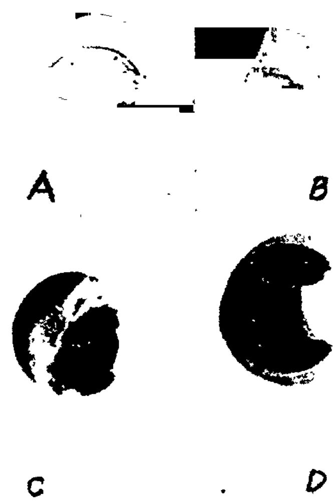

Fig. 5.—Steps of transurethral resection shown by endoscopic photographs. *A*, cutting loop in position for cut in roof of urethra. *B*, groove after resection of first bite of tissue; *C*, lateral wall of vesical neck during cutting of section of tissue; *D*, groove in lateral wall after cut has been completed.

It is important to explain to each patient that healing of her resected urethra will require six to eight weeks or more. She may expect to experience dysuria, pain, urgency, and some hematuria during this healing period. Urethral suppositories, urethral dilations, and injections of Argyrol or other soothing medicaments are given during office follow-up treatments, usually at intervals of one to two weeks. Sulfonamides and other urinary antiseptics are prescribed to lessen the urinary infection during convalescence. The urine usually is free from infection within 8 to 10 weeks after the transurethral resection.

On dismissal, patients are advised to come back at intervals of 2 to 3 months for a period up to about 12 months. Cystourethroscopic inspection of each patient is done about 10 to 12 weeks postoperatively. At this time, light fulguration of any area of inflamed posterior urethra that is noticed often is of benefit. Such "touch-up" fulgurations have been helpful, in many instances. We have found that a special electrode guide for use with the panendoscope is quite useful in these touch-up fulgurations as well as in any instance requiring electrofulguration.

Summary

The urethritis-cystitis syndrome is a common malady in women. Many of these patients have been neglected in the past, and others have been labeled "neurotic." A carefully taken history and examination, especially calibration of the urethra with an Otis bougie à boule and penendoscopic inspection of the entire urethra and vesical neck reveal the true nature of this urethritis and cystitis to be obstructive in most instances. Meatotomy with elimination of infected urethral glands, dilations of strictures, and transurethral resection of the bladder neck have given a high percentage of satisfactory results in more than 2,500 patients seen during the past 15 years.

The special electrode guide for use with the panendoscope used in this study was devised and supplied by Mr. Fred Wallace of American Cystoscope Makes, Inc.

COMPLETE SYSTEM FOR ELECTROCARDIOGRAM PROCESSING APPLICABLE TO MECHANICAL SORTING

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The purpose of the system here described is to expedite the filing, recall, and study of electrocardiograms by the use of punch cards and a code. The three basic components of the system are a combination request, interpretation, and billing form, a standard punch card, and a four-digit code. The code supplies a number to match every possible electrocardiographic diagnosis. Since each punch card has 80 columns, there is room for 17 boxes of four digits each, to represent as many as 17 different diagnoses, in addition to necessary identifying data. Experience with the processing of more than 14,000 electrocardiograms showed that this system greatly increases the speed and ease with which records of individual patients are recalled or large numbers of records are studied for research purposes.

Although many electrocardiogram coding systems are in use on a regional basis none has achieved national acceptance. It is obvious that if standardization of nomenclature and codes for diagnoses could be accomplished the transmission of electrocardiographic information would be greatly facilitated. This is especially clear when one considers the new electronic equipment which has become available to sort and classify information. Most of these machines must utilize digital systems for data processing. This communication describes a single, digital electrocardiogram coding system which lends itself to both manual and mechanical sorting. The use of mechanical sorting has become commonplace in many areas of industry and health, but a search of the literature fails to reveal the publication of such a digital system applicable to electrocardiogram coding. In fact, other than those systems contained

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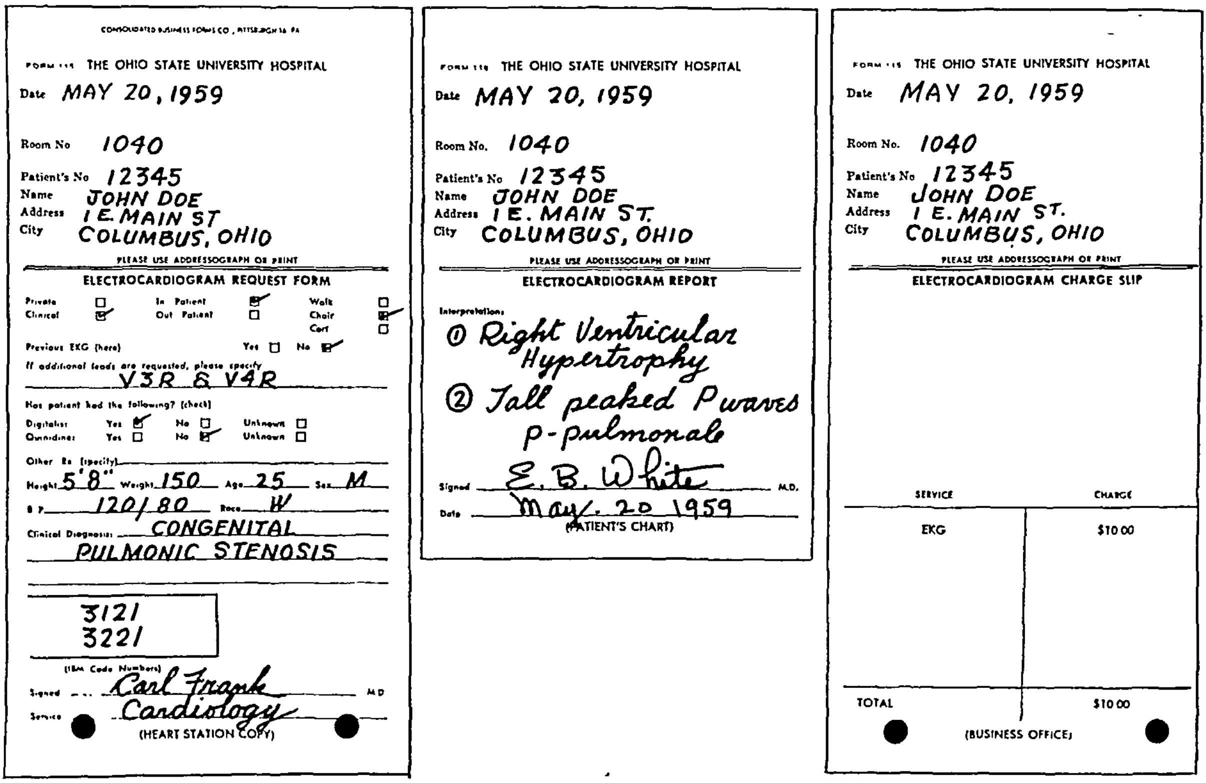
in standard textbooks,[1] publications dealing with coding methods of any type are notably absent from the current literature.

The System

The complete electrocardiogram processing system herein described consists essentially of three basic components, which will be described sequentially.

Combination Request, Interpretation, and Billing Form.—The combination request, interpretation, and billing form (fig. 1) is a three-piece, tear-away type form, with carbon backing over the name plate area on the first two sheets. The first sheet contains that information which will be of aid in the interpretation of the electrocardiogram, together with a box in the lower left-hand corner in which the appropriate code numbers of this particular electrocardiogram can be entered. The second sheet is used for sending the interpretation back to the hospital floor or the ordering physician, and the third sheet is used for billing purposes.



CONSOLIDATED BUSINESS FORMS CO., PITTSBURGH 16, PA

FORM 115 THE OHIO STATE UNIVERSITY HOSPITAL

Date MAY 20, 1959

Room No 1040

Patient's No 12345
Name JOHN DOE
Address 1 E. MAIN ST
City COLUMBUS, OHIO

PLEASE USE ADDRESSOGRAPH OR PRINT

ELECTROCARDIOGRAM REQUEST FORM

Private ☐ In Patient ☑ Walk ☐
Clinical ☑ Out Patient ☐ Chair ☑
Cart ☐

Previous EKG (here) Yes ☐ No ☑

If additional leads are requested, please specify V3R & V4R

Has patient had the following? (check)
Digitalis: Yes ☑ No ☐ Unknown ☐
Quinidine: Yes ☐ No ☑ Unknown ☐

Other Rx (specify)

Height 5'8" Weight 150 Age 25 Sex M

B.P. 120/80 Race W

Clinical Diagnosis: CONGENITAL PULMONIC STENOSIS

3121
3221

(IBM Code Numbers)

Signed Carl Frank M.D.

Service Cardiology

(HEART STATION COPY)

FORM 115 THE OHIO STATE UNIVERSITY HOSPITAL

Date MAY 20, 1959

Room No. 1040

Patient's No 12345
Name JOHN DOE
Address 1 E. MAIN ST.
City COLUMBUS, OHIO

PLEASE USE ADDRESSOGRAPH OR PRINT

ELECTROCARDIOGRAM REPORT

Interpretation:
① Right Ventricular Hypertrophy
② Tall peaked P waves p-pulmonale

Signed E. B. White M.D.

Date May. 20 1959

(PATIENT'S CHART)

FORM 115 THE OHIO STATE UNIVERSITY HOSPITAL

Date MAY 20, 1959

Room No. 1040

Patient's No 12345
Name JOHN DOE
Address 1 E. MAIN ST.
City COLUMBUS, OHIO

PLEASE USE ADDRESSOGRAPH OR PRINT

ELECTROCARDIOGRAM CHARGE SLIP

SERVICE	CHARGE
EKG	$10.00
TOTAL	$10.00

(BUSINESS OFFICE)

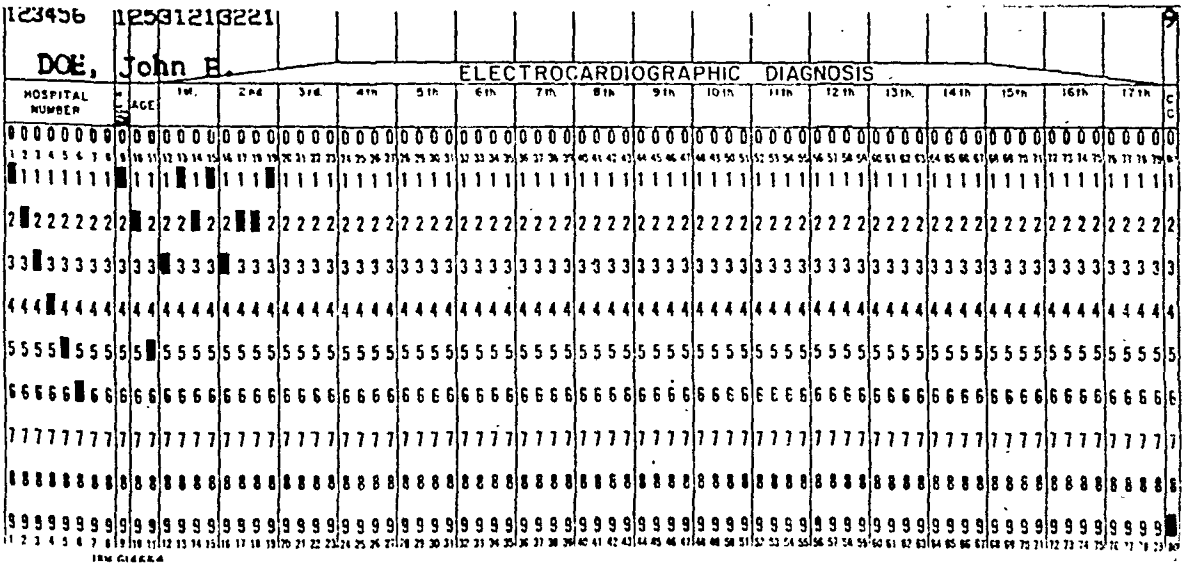
Fig. 1.—From left to right: pages one, two, and three of combination request, interpretation, and billing form of electrocardiogram coding system.

On receipt of a properly completed form an electrocardiogram is taken in the heart station. The complete electrocardiogram request form without the third or billing sheet is attached to the mounted electrocardiogram, together with an IBM code card (fig. 2), if the patient has had previous electrocardiograms taken. After interpretation of the electrocardiogram the diagnoses are written on the mount of the tracing together with the proper code numbers. These code numbers then are transcribed by the secretary to the box on the lower left-hand corner on the first of the three sheets of the request form. The interpretation is typed on the second sheet, and this is returned to the physician or the hospital floor. On the back of the IBM code card the date of the electrocardiogram is typed in together with the appropriate coded diagnoses, and the patient's name is typed on the front of the card. Next, the first sheet is sent to the IBM coding section with this new IBM code card or, if a previous electrocardiogram has been taken, a previously punched IBM code card. After the IBM punch operator enters the proper digits on the card it is returned to the secretary of the heart station and filed numerically in the current weekly file. The electrocardiogram is also filed by hospital or unit number. All electrocardiograms taken of one person are bound together, usually by a rubber band.

IBM Card.—The second part of the system consists of the IBM card itself (fig. 2), on the face of which the following columns for data have been imprinted: hospital number, race and sex, age, and 17 boxes of four digits each which include electrocardiographic diagnoses (table 1). The method used for coding race and sex is as follows: (1) white male, (2) white female, (3) nonwhite male, and (4) nonwhite female. Age is entered in columns 11 and 12. Although we have used the patient's age at the time his first electrocardiogram was taken, entering the patient's year of birth might be preferable. Under our system the unit or hospital number is used throughout. If the patient has not had a previous number one is obtained from the record room. An auxiliary filing system for correlation of the patient's name, which is in alphabetical order, with the unit number would be optional. The current, punched IBM cards are kept in a separate drawer and taken down to the IBM section for merging at variable intervals, depending on the volume of tracings taken, but usually once a week. That is to say, they are placed in numerical sequence in their proper order in the master file. All IBM cards are kept in the heart station in special filing cabinets. When a new electrocardiogram is taken on a patient who has previously had one, this card is pulled out and attached to this latest electrocardiogram, so that all old diagnoses are immediately available. If a question arises the old electrocardiograms can then be pulled out without difficulty. It has been our practice to punch a single diagnosis only once, regardless of how many times this diagnosis recurs on subsequent electrocardiograms. In this way 17 separate diagnoses can be entered on one card, so that most patients have no more than one card on file. For example, if a patient's diagnosis is left ventricular hypertrophy, i. e., 3111, this digital series will appear on the IBM code card only once, no matter the number of electrocardiograms taken which have this same diagnosis. The mechanical sorter will always pull out this record on request. Special mention should also be made of column 80, in which we place the last digit of the year of the earliest electrocardiogram taken on a given person. For example, if the patient's first electrocardiogram was taken in 1952, a 2 could appear in column 80. This system has been devised for the retiring of old electrocardiograms to either microfilming or destruction, whichever seems appropriate. It has been our practice to retire these electrocardiograms after nine years, so that, for example, in 1961 all those electrocardiograms with a 2 appearing in column 80 would be pulled out and appropriate action taken. The cards would then be updated to the date of the next-to-the-oldest electrocardiogram taken on this person.

TABLE 1.—*IBM Card Data of Electrocardiogram Coding System*

IBM Columns	*Information*
1 through 8	Hospital number
9	Race and sex
11 and 12	Age
13 through 79	Electrocardiogram diagnoses
80	Retiring number


123456 1253121 3221 9

DOE, John B.

ELECTROCARDIOGRAPHIC DIAGNOSIS
HOSPITAL NUMBER
AGE
1st
2nd
3rd
4th
5th
6th
7th
8th
9th
10th
11th
12th
13th
14th
15th
16th
17th
IBM G14664

Fig. 2.—Punched and plate-imprinted IBM code card of electrocardiogram coding system.

Four-Digit Code System.—The third part of the system is the four-digit code system (table 2). This system is divided into eight primary numbers, with secondary and tertiary subdivisions of these primary numbers. The fourth digit, in all cases, is a modifying digit; this is seen in the lower right-hand corner of the table and refers to the certainty of the diagnosis, to the presence of serial changes, and the like. Typical examples of electrocardiographic diagnoses would be as follows: (1) definite atrial fibrillation, 2631; or (2) probable old anterior myocardial infarction, 5132. For most diagnoses this system is self-explanatory. Problems arise occasionally in the area of rhythms when, for example, one may have to code atrial tachycardia with constant 2:1 block. This is coded in the following manner: 2611; 4231. If a patient previously had an arrhythmia which now has reverted to normal sinus rhythm, the diagnosis of the arrhythmia is recorded

14,000 records have been processed. We have found it to be of definite value in the simplification of the routine handling of ordering, coding, and filing of electrocardiograms. In addition, it makes the recall of electrocardiograms for research purposes a simple and rapid process. For example, at present we have in our system some 14,000 coded electrocardiograms. All of these cards, which contain a specific diagnosis, a combination of various diagnoses, or information such as age by decade or other items, could be sorted in two to three hours and placed in numerical sequence for easy pulling of the filed tracings.

Considerable controversy rages at present over terminology with respect to electrocardiographic diagnoses. In practice, however, some rewording of the terminology would not interfere with use *in toto* of the described system—provided, of course, the code numbers were not changed. This complete system for the requesting, coding, filing, and recall of electrocardiograms lends itself to either mechanical or manual sorting processes.

Heart Station, Ohio State University Hospital (10) (Dr. Booth).

We wish to express our appreciation to Mrs. Jo Ann Martin, Miss Gloria Meeks, and Mr. Fred Shepard for technical assistance.

References

1. Barker, J. M., and Wallace, J. J.: Unipolar Electrocardiogram: Clinical Interpretation, New York, Appleton-Century-Crofts, Inc., 1952. Katz, L. N., and Pick, A.: Clinical Electrocardiography. Part I: Arrhythmias with Atlas of Electrocardiograms, Philadelphia, Lea & Febiger, 1956.

THE CHRONIC ALCOHOLIC

Fitzhugh C. Pannill, M.D., Corsicana, Texas
and
Jackson A. Smith, M.D., Omaha, Neb.

Treatment for the chronic alcoholic, after a prolonged bout of alcohol ingestion, must attempt to correct the effects of alcohol on the central nervous system and gastrointestinal tract, the possible damage to the liver, and any existing malnutrition. The patient is best managed in the hospital, where complete control can be maintained during the period of withdrawal. Water, electrolytes, glucose, and vitamins are administered intravenously until the patient is able to eat. Understanding of the patient's dilemma rather than an attitude of rejection is necessary for rehabilitation.

The treatment of the alcoholic may be divided into two phases: first, the management of the patient immediately after a bout and, later, an effort to prevent his resuming the previous drinking pattern. The first phase of treatment is primarily medical and may constitute a medical emergency. The later efforts may be principally concerned with the emotional aspects of the patient's difficulties and are less somatic than psychiatric treatment.

This paper is primarily concerned with the correction of those changes which follow a prolonged period of an excessive intake of alcohol. The maintenance of sobriety after a bout of drinking will be briefly mentioned.

Metabolism of Alcohol

Alcohol has been used as a tranquilizing agent during the 5,000 years of recorded history and was known to produce tranquillity to the point of stupor long before man was aware that the phenothiazines had derivatives. It has been officially accepted as a medical problem, and it has been recommended by the American Medical Association that alcoholic patients be admitted to general hospitals without the barrier of diagnostic exclusion. The only one of the alcohols considered here is ethyl alcohol, since the others are too immediately toxic to present a great problem. Alcohol has been known to have both antiseptic and anesthetic properties for a number of years. In fact, it has been used by the British Army as an anesthetic, but there [illegible]stitute
margin of safety in its use and [illegible]essing drug, alco-
abolishing reflexes or prod[illegible]tolerate.
of muscle relaxation.[1] [illegible]s for immediately discon-

Alcohol taken ora[illegible]h a patient; the first being the
the stomach and t[illegible]bstance on hi[illegible]ready damaged
nal tract. The r [illegible] increased [illegible] gical de-
by seve[illegible] [illegible]m its
substa[illegible] as [illegible] is a [illegible] is
part[illegible] that [illegible] m [illegible]
[illegible]ol over [illegible] id
[illegible]f superi
the great

From the Medical Arts Clinic, Corsicana, Texas and the Nebraska Psychiatric Institute, Omaha.

once more and a 5, indicating serial changes, is placed in the fourth digit. For example, for a patient with previous atrial fibrillation and a now normal sinus rhythm the code would be 2631 on the first electrocardiogram and 2635 on the subsequent electrocardiogram, showing normal sinus rhythm.

Comment.—The system here described, as previously noted, lends itself to both manual and mechanical sorting. Where manual use of this system is desired it is necessary to place the digits of the diagnoses on file cards. These could be filed alphabetically by name or numerically by unit number. It is also necessary to keep a master book, the pages of which are headed by the various digital diagnoses. It is on these pages that the unit numbers of the electrocardiograms falling under each given category next are written.

Table 2.—*Four-Digit IBM Electrocardiographic Code*

1. Normals, Sinus Mechanisms
   1. Sinus rhythm
      1. Normal
      2. Sinus tachycardia
      3. Sinus bradycardia
      4. Sinus arrhythmia
      5. Normal infant
      6. Normal child
   2. Sinus
      1. Arrest
      2. Premature systoles
      3. Wandering pacemaker
      4. Block (SA)
      5. Ventriculophasic sinus arrhythmia

2. Arrhythmias: Premature Systoles
   1. Atrial
   2. AV nodal
   3. Supraventricular
   4. Ventricular
   5. Site unknown

      1. Premature systoles (usual)
      2. Coupled
      3 Trigeminal
      4. Interpolated
      5. Multifocal
      6. Fusion
      7. Antegrade block (atrial or nodal) or retrograde conduction (ventricular)
      8. Parasystole
      9. Reentry

Arrhythmias: Rhythms
   6. Atrial
   7. AV nodal
   8. Supraventricular
   9. Ventricular

      1. Tachycardia
      2. Flutter
      3. Fibrillation
      4. Rhythm
      5. Wandering pacemaker
      6. Escape
      7. Arrest
      8. Retrograde AV block
   0. Miscellaneous
      1. Reciprocal rhythm
      2. Abnormal rhythm, type undetermined
      3. Aberration of QRS
      4. Retrograde atrial conduction
      5. Mechanical stimulation of atrium

3. Ventricular Hypertrophy and P-Wave Abnormalities
   1. Ventricular hypertrophy
      1. Left
      2. Right
      3. Combined
   2. P waves
      1. Notched
      2. Peaked
      3. Broad

4. Conduction Abnormality
   1. S-A
      1. Block
      2. Wenckebach
   2. A-V
      1. Prolonged PR—constant
      2. Prolonged PR—inconstant
      3. Partial block—constant
      4. Partial block—inconstant
      5. Complete block with nodal rhythm
      6. Complete block with idioventricular rhythm
   3. A-V
      1. Concealed conduction
      2. A-V dissociation (complete with atrial rate less than ventricular rate)
      3. Wenckebach phenomenon
      4. Dissociation with interference
      5. Accelerated A-V conduction
      6. Wolff-Parkinson-White syndrome
      7. Supernormal phase of conduction
      8. Capture
   4. Intraventricular
      1. Incomplete right bundle-branch block
      2. Complete right bundle-branch block
      3. Incomplete left bundle-branch block
      4. Complete left bundle-branch block
      5. IV conduction defect, type undetermined
      6. Peri-infarction block
      7. Left intraventricular conduction defect (parietal block)

5. Myocardial Infarction
   1. Anterior
   2. Anteroseptal
   3. Anterolateral
   4. High-lateral
   5. Posterior
   6. High-posterior
   7. Transeptal-posterior
   8. Apical
   9. Subendocardial
   0. Posterolateral

      1. Fresh
      2. Recent
      3. Old
      4. Age undetermined

6. Abnormalities of Repolarization
   1. ST-T wave changes
      1. Nonspecific (usual)—some of which may be due to digitalis
      2. Nonspecific (usual)—due to digitalis
      3. Wide QRS-T angle only
      4. Borderline (not definitely abnormal)
      5. Secondary to rate
      6. Post-tachycardia
      7. Tall-peaked T waves—cause unknown
      8. Localized T-wave inversion—anterior
      9. Persistent juvenile pattern
   2. Ischemia (symmetrical T-wave inversion)
      1. Anterior
      2. Posterior
   3. ST segment displacement
      1. Subendocardial injury
      2. Epicardial injury (other than pericarditis)
      3. Site of injury unknown
      4. Ventricular aneurysm
      5. Definite displacement, probably not due to injury
   4. Pericarditis
      1. Acute
      2. Subacute
      3. Chronic

7. Changes due to Drugs, Electrolytes, Inflammation, and Related Phenomena (U Wave)
   1. Drugs
      1. Digitalis
      2. Quinidine
      3. Procainamide hydrochloride
      4. Other
   2. Electrolyte imbalance
      1. Hypopotassemia
      2. Hyperpotassemia
      3. Hypocalcemia
      4. Hypercalcemia
      5. Other (combined, etc.)
   3. Nonspecific (or cause uncertain)
      1. Prolonged electrical systole
      2. Prominent U wave
   4. Myocarditis (myocardosis)
      1. Rheumatic
      2. Viral
      3. Other
      4. Unknown (e. g., Friedreich's)

8. Miscellaneous
   1. Low voltage
      1. Limb leads only
      2. Precordial leads only
      3. Entire record
   2. Exercise test
      1. Normal
      2. Abnormal
      3. Borderline
   3. Positional
      1. Left axis deviation
      2. Right axis deviation
      3. Clockwise rotation
      4. Counter-clockwise rotation
      5. Dextrocardia
      6. Aberrant position (anatomic)
   4. Changes secondary to pulmonary disease
      1. Consistent with cor pulmonale
      2. Consistent with pulmonary infarction
   5. Other
      1. Electrical alternans
      2. Myocardial trauma (clinical)
      3. Terminal EKG
   6. Dead
      1. Autopsy
      2. No autopsy
      3. Unknown
   7. Special leads taken
      1. V3R & V4R (right precordial leads)
      2. Special V leads (left precordial)
      3. Extra leads for rhythm
      4. Esophageal leads
      5. With inspiration and expiration (III & aVF)
      6. Patient sitting up (III & aVF)

4th Digit
   1. Definite
   2. Probable
   3. Possible
   4. Serial changes
   5. Transient, variable degree (I.V. conduction defect) intermittent, onset and/or offset
   6. Changes as in 5 but due to special procedures
   7. Unusual record from teaching standpoint

The mechanical sorting system in use at Ohio State University Hospital consists of the following four units: 1. An IBM card punch which enters the appropriate data on each card. 2. An IBM verifier which verifies the correctness of the punched information. 3. A 101 sorter. This instrument is capable of sorting 27,000 cards per hour and handling up to 12 characters on a single pass through the machine. 4. A collator which blends new cards into their proper numerical order in the master system and also indicates the presence of duplicate cards. Usually three passes of our cards are necessary to extract the desired information.

Summary and Conclusions

The system for processing electrocardiograms herein described has been in use at Ohio State University Hospital for almost two years, and over

14,000 records have been processed. We have found it to be of definite value in the simplification of the routine handling of ordering, coding, and filing of electrocardiograms. In addition, it makes the recall of electrocardiograms for research purposes a simple and rapid process. For example, at present we have in our system some 14,000 coded electrocardiograms. All of these cards, which contain a specific diagnosis, a combination of various diagnoses, or information such as age by decade or other items, could be sorted in two to three hours and placed in numerical sequence for easy pulling of the filed tracings.

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margin of safety in its use and pressing drug, alco
abolishing reflexes or prod tolerate.
of muscle relaxation.[1] us for immediately disco

Alcohol taken ora h a patient; the first being t
the stomach and t ubstance on his already damag
nal tract. The r the increased psychological
enced by severe drug from its medical use.
other substar as first seen is a pitiful sight. It
tion is part that the physician must exert all pc
Alcohol rol over himself to avoid an instincti
tion is bf superiority over the patient. This
about t the greatest barrier to successful trea

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      6. Normal child
   2. Sinus
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      4. Block (SA)
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   2. AV nodal
   3. Supraventricular
   4. Ventricular
   5. Site unknown

      1. Premature systoles (usual)
      2. Coupled
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      4. Interpolated
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      9. Reentry

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   7. AV nodal
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   9. Ventricular

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      3. Fibrillation
      4. Rhythm
      5. Wandering pacemaker
      6. Escape
      7. Arrest
      8. Retrograde AV block
   0. Miscellaneous
      1. Reciprocal rhythm
      2. Abnormal rhythm, type undetermined
      3. Aberration of QRS
      4. Retrograde atrial conduction
      5. Mechanical stimulation of atrium

3. Ventricular Hypertrophy and P-Wave Abnormalities
   1. [illegible]
      1. Left
      2. Right
      3. Combined
   2. P waves
      1. Notched
      2. Peaked
      3. Broad

4. Conduction Abnormality
   1. S-A
      1. Block
      2. Wenckebach
   2. A-V
      1. Prolonged PR—constant
      2. Prolonged PR—inconstant
      3. Partial block—constant
      4. Partial block—inconstant
      5. Complete block with nodal rhythm
      6. Complete block with idioventricular rhythm
   3. A-V
      1. Concealed conduction
      2. A-V dissociation (complete with atrial rate less than ventricular rate)
      3. [illegible]
      4. [illegible]
      5. [illegible]
      6. [illegible]
      7. [illegible]
      8. Capture
   4. Intraventricular
      1. Incomplete [illegible]
      2. Complete [illegible]
      3. Incomplete [illegible]
      4. Complete left bundle-branch block
      5. IV conduction defect, type undetermined
      6. Peri-infarction block
      7. Left intraventricular conduction defect (parietal block)

5. Myocardial Infarction
   1. Anterior
   2. Anteroseptal
   3. Anterolateral
   4. High-lateral
   5. Posterior
   6. High-posterior
   7. Transeptal-posterior
   8. Apical
   9. Subendocardial
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      1. Fresh
      2. Recent
      3. Old
      4. Age undetermined

6. Abnormalities of Repolarization
   1. ST-T wave changes
      1. Nonspecific (usual)—some of which may be due to digitalis
      2. Nonspecific (usual)—due to digitalis
      3. Wide QRS-T angle only
      4. Borderline (not definitely abnormal)
      5. Secondary to rate
      6. Post-tachycardia
      7. Tall-peaked T waves—cause unknown
      8. Localized T-wave inversion—anterior
      9. Persistent juvenile pattern
   2. Ischemia (symmetrical T-wave inversion)
      1. Anterior
      2. Posterior
   3. ST [illegible]
      1. [illegible]
      2. [illegible] than pericarditis)
      3. Site of injury unknown
      4. Ventricular aneurysm
      5. Definite displacement, probably not due to injury
   4. Pericarditis
      1. Acute
      2. Subacute
      3. Chronic

7. Changes due to Drugs, Electrolytes, Inflammation, and Related Phenomena (U Wave)
   1. Drugs
      1. Digitalis
      2. Quinidine
      3. Procainamide hydrochloride
      4. Other
   2. Electrolyte imbalance
      1. Hypopotassemia
      2. Hyperpotassemia
      3. Hypocalcemia
      4. Hypercalcemia
      5. Other (combined, etc.)
   3. Nonspecific (or cause uncertain)
      1. Prolonged electrical systole
      2. Prominent U wave
   4. Myocarditis (myocardosis)
      1. Rheumatic
      2. Viral
      3. Other
      4. Unknown (e. g., Friedreich's)

8. Miscellaneous
   1. Low voltage
      1. Limb leads only
      2. Precordial leads only
      3. Entire record
   2. Exercise test
      1. Normal
      2. Abnormal
      3. Borderline
   3. Positional
      1. *Left axis deviation*
      2. Right axis deviation
      3. Clockwise rotation
      4. Counter-clockwise rotation
      5. Dextrocardia
      6. Aberrant position (anatomic)
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      1. Consistent with cor pulmonale
      2. Consistent with pulmonary infarction
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      1. Electrical alternans
      2. Myocardial trauma (clinical)
      3. Terminal EKG
   6. Dead
      1. Autopsy
      2. No autopsy
      3. Unknown
   7. Special leads taken
      1. V3R & V4R (right precordial leads)
      2. Special V leads (left precordial)
      3. Extra leads for rhythm
      4. Esophageal leads
      5. With inspiration and expiration (III & aVF)
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   6. Changes as in 5 but due to special procedures
   7. Unusual record from teaching standpoint

The mechanical sorting system in use at Ohio State University Hospital consists of the following four units: 1. An IBM card punch which enters the appropriate data on each card. 2. An IBM verifier which verifies the correctness of the punched information. 3. A 101 sorter. This instrument is capable of sorting 27,000 cards per hour and handling up to 12 characters on a single pass through the machine. 4. A collator which blends new cards into their proper numerical order in the master system and also indicates the presence of duplicate cards. Usually three passes of our cards are necessary to extract the desired information.

Summary and Conclusions

The system for processing electrocardiograms herein described has been in use at Ohio State University Hospital for almost two years, and over

14,000 records have been processed. We have found it to be of definite value in the simplification of the routine handling of ordering, coding, and filing of electrocardiograms. In addition, it makes the recall of electrocardiograms for research purposes a simple and rapid process. For example, at present we have in our system some 14,000 coded electrocardiograms. All of these cards, which contain a specific diagnosis, a combination of various diagnoses, or information such as age by decade or other items, could be sorted in two to three hours and placed in numerical sequence for easy pulling of the filed tracings.

Considerable controversy rages at present over terminology with respect to electrocardiographic diagnoses. In practice, however, some rewording of the terminology would not interfere with use in terms of the described system, provided, of course, the code numbers were not changed. This complete system for the requesting, coding, filing, and recall of electrocardiograms lends itself to either mechanical or manual sorting processes.

Heart Station, Ohio State University Hospital (10) (Dr. [illegible]).

We wish to express our appreciation to Mrs. Jo Ann Martin, Miss Glenn Meeks, and Mr. Fred Shepard for technical assistance.

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THE CHRONIC ALCOHOLIC

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Treatment for the chronic alcoholic, after a prolonged bout of alcohol ingestion, must attempt to correct the effects of alcohol on the central nervous system and gastrointestinal tract, the possible damage to the liver, and any existing malnutrition. The patient is best managed in the hospital, where complete control can be maintained during the period of withdrawal. Water, electrolytes, glucose, and vitamins are administered intravenously until the patient is able to eat. Understanding of the patient's dilemma rather than an attitude of rejection is necessary for rehabilitation.

The treatment of the alcoholic may be divided into two phases: first, the management of the patient immediately after a bout and, later, an effort to prevent his resuming the previous drinking pattern. The first phase of treatment is primarily medical and may constitute a medical emergency. The later efforts may be principally concerned with the emotional aspects of the patient's difficulties and are less somatic than psychiatric treatment.

This paper is primarily concerned with the correction of those changes which follow a prolonged period of an excessive intake of alcohol. The maintenance of sobriety after a bout of drinking will be briefly mentioned.

Metabolism of Alcohol

Alcohol has been used as a tranquilizing agent during the 5,000 years of recorded history and was known to produce tranquillity to the point of stupor long before man was aware that the phenothiazines had derivatives. It has been officially accepted as a medical problem, and it has been recommended by the American Medical Association that alcoholic patients be admitted to general hospitals without the barrier of diagnostic exclusion. The only one of the alcohols considered here is ethyl alcohol, since the others are too immediately toxic to present a great problem. Alcohol has been known to have both antiseptic and anesthetic properties for a number of years. In fact, it has been used by the British Army as an anesthetic, but there is [illegible]
margin of safety in its use an
abolishing reflexes or pro
of muscle relaxation.[1] a

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From the Medical Arts Clinic, Corsicana, Texas and the Nebraska Psychiatric Institute, Omaha.

After absorption, alcohol passes via the portal vein to the liver, on to the vena cava, to the heart and lungs, and then into the arterial circulation. Some delay is noted in the rise of the level of the cerebrospinal fluid and there is also a delay in the fall in the level in this medium. Alcohol is present, shortly, in all the tissues and in both intracellular and extracellular fluids. Alcohol is metabolized as a linear function of time but not of concentration, and about 1 oz. of whiskey is the maximum that can be metabolized in an hour. The maximum amount that can be metabolized daily is approximately 380 cc. of alcohol, the excess being circulated until it is metabolized. Ninety per cent of the alcohol is destroyed by oxidation, while the remaining 10% is excreted unchanged by renal, pulmonary, and cutaneous routes.

The oxidation of 1 Gm. of alcohol yields 7 calories, with carbon dioxide and water as the end-products. This process begins immediately on absorption and continues as long as any alcohol remains in the organism.

The liver is the primary site of oxidation of alcohol and the process has been studied extensively in vitro and in vivo.[2] Alcohol dehydrogenases are the enzymes responsible for the reaction and the coenzyme is diphosphopyridine nucleotide (DPN). During the metabolism of alcohol, blood entering and leaving the liver shows a rise in pyruvic and lactic acid levels which results in a mild acidosis. Removal of pyruvic acid and the accumulation of reduced DPN leads to a reduction in the citric acid cycle and a reduced reservoir of adenosinetriphosphate (ATP). This oxidation by dehydrogenation proceeds so rapidly that the hydrogen ion and electron acceptors are depleted and the ATP dependent reactions are slowed or temporarily halted. The conversion of acetaldehyde to acetic acid may take place in other organs and some excretion of this product in this form may occur. Once alcohol is transformed to acetic acid the reaction is universal throughout the tissues and becomes a part of the tricarboxylic acid (Krebs') cycle. The nonmetabolic excretion of alcohol is minimal and variable, but equilibrium between blood and alveolar air is the basis for clinical tests of intoxication.

Pharmacologically, alcohol acts as a depressant drug on the central nervous system; this depression
the concentration rises until eventually
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are reached; and the cardiovascular effects are minimal, although a moderate intake does produce a cutaneous vasodilatation with a sense of warmth. The dilating effects on the coronary arteries and the cerebral vessels are minimal. A 10% solution of alcohol produces an increase in both volume and acidity of the gastric contents. As the concentration of the alcohol rises, the secretion is inhibited. Higher concentrations of alcohol produce hyperemia and inflammation of the gastric mucosa and concentrations above 30% interfere with absorption. This also accounts for the "alcoholic gastritis" seen after an acute bout and is present in about one-third of those persons with chronic alcoholism. The intestinal changes seen are ordinarily due to substances other than the alcohol, such as irritating oils or other congeners. Alcohol taken to the point of intoxication produces a cessation of all gastrointestinal secretory and motor functions. The liver and pancreas are not affected by small amounts of alcohol. However, alcohol does produce a specific diuretic effect on the kidneys in the form of a water diuresis. For instance, 14 cc. of 86-proof whiskey produces a consistent water diuresis for two hours, with no change in sodium, potassium, or chloride concentration. This may be inhibited by pitressin and sodium chloride. This diuresis probably results from the action of alcohol on a supraoptic hypophysial system to inhibit the secretion of posterior pituitary antidiuretic hormone.[4]

Alcohol apparently has no effect on skeletal muscle, and the increased ability to work sometimes seen is probably the effect of the failure to perceive fatigue. Diplopia may result from poor muscular coordination and nystagmus may be due to a cerebellar effect, while emesis may result from both local and central nervous system effects.

General Effects

There is a decrease in the alkali-binding power of the blood, and alveolar hypoventilation produces carbon dioxide retention. The accumulation of lactic acid and acetic acid further diminish the alkali reserve. Since the acetaldehyde is metabolized slowly, the disturbance is prolonged and continues as one of the toxic factors after an acute bout of drinking.[2a]

In the hang-over, the headache may be due to both toxic and vascular effects, the vertigo is probably of central nervous system origin, and the nausea and emesis are caused by both central and peripheral effects. The hematological and electrolyte effects are those seen and expected as secondary to the accompanying dehydration.

The effects on cholesterol metabolism are interesting, since in most chronic alcoholics the cholesterol level is found at the lower limits of normal. The ingestion of alcohol produces no demonstrable change in the nonalcoholic drinker. The level of cholesterol esters is lowered in parenchymal liver damage, although cholesterol is more easily synthesized from acetic acid than from acetate substrates.[5]

The most consistent, frequent pathological change in persons with chronic alcoholism is in the liver. Leevy and others[6] found in the results of biopsies of the livers of 66 chronic alcoholics with delirium tremens that about one-third had a normal liver, another third had a fatty liver, and the final third had portal cirrhosis. He found no correlation between severity and duration of delirium tremens and histological changes, nor was there any correlation between the hepatic abnormalities and the amount or type of alcohol the person had drunk. There was a correlation between the liver changes and the dietary habits. He was not able to correlate the clinical signs with the anatomic findings, but he believed that alcohol caused an increased need for lipotropic substances and that the combination of alcoholism and dietary deficiency provided the proper substrate for the development of a fatty liver. It has been found that 75% of all alcoholics have fatty livers[7] and that only 9 out of 100,000 persons at large die from cirrhosis, whereas 650 out of 100,000 chronic alcoholics die of cirrhosis.[8]

Patients with liver insufficiency have been found to have a significant reduction in cerebral oxygen consumption in spite of the fact that there are no evident neurological signs.[2a] Mild inebriation produces no effects on cerebral blood flow, metabolism, or vascular resistance if there is no concurrent liver disease.

Leevy[6a] found that fatty livers were most marked in patients on carbohydrate diets lacking in lipotropic factors, but hepatomegaly was a finding observed in 80% of patients. Anorexia, nausea, vomiting, diarrhea, capillary dilatation, loss of weight, malnutrition, cachexia, personality changes, delirium tremens, mental and moral deterioration, cirrhosis, pellagra, polyneuritis, optic atrophy, psychoses, and multiple related organic disorders due to lowered vitality and resistance are some of the varied signs and symptoms of the chronic alcoholic. Most of these problems are not encountered in the chronic alcoholic whose food consumption and assimilation are adequate, but this is not often the case. The calories supplied by the alcohol diminish the food intake as well as the appetite. A heavy drinker may supply one-half of his total calories in alcohol and this may continue for many years. The above-named deficiency diseases, a lowered resistance to infection, and susceptibility to trauma may occur with increasing frequency in the chronic alcoholic.

The experimental production of the fatty liver has yielded some pertinent facts. A deficiency of methyl group donors (choline, betaine, B_{12}, folic acid, citrovarum factor) will produce a fatty liver with later development of cirrhosis.[9] Necrosis of the liver with widespread hepatic parenchymal degeneration is produced by a deficiency of amino acids (cystine, selenium, methionine, vitamin E). In the production of either fatty liver or hepatic necrosis, the greater the caloric intake the greater the effect of the vitamin deficiency. Alcohol provides an excess of calories which causes an imbalance between calories and proteins or lipotropic substances, and thus serves to intensify the deficiency already existing.

The problem of hepatic coma has presented an interesting paradox in the treatment of the chronic alcoholic. It has been observed that chronic alcoholics who are given ammonium-containing medicaments (NH_4Cl, urea, resins) soon develop mental confusion and a "flapping" tremor.[10] These changes are reversible on discontinuance of the medication. The same phenomenon was observed in animals with an Eck fistula who were given high-protein diets, and subsequently it has been demonstrated that blood ammonia levels above normal range (40 to 60 mg.%) occur in persons with these cerebral abnormalities.[11] In certain critical situations, the intestinal flora may produce enough ammonium to cause coma-like symptoms, and hence the improvement observed after administration of broad-spectrum antibiotics. Attempts to correct the problem of hepatic coma have consisted of giving glutamic acid (to combine with the excess ammonia as glutamine) and arginine (to act as a precursor of ornithine in priming the Krebs-Hensleit urea cycle).[12] Patients with reversible hepatic coma have been treated by both of these methods, with some success. The physician who treats this form of liver failure must recognize the contradictory problems raised by the intolerance for proteins and the need for protein realimentation. During the last stages of liver failure, protein is virtually lethal, hence it must be determined at which point small amounts of protein may be given with sufficient nonprotein calories to spare immediate deamination of this material. With proper management, hypoproteinemia, ascites, and edema may improve. The tolerance for amino acids and for glucose may return toward normal, and the metabolism of galactose, bile pigments, steroids, and thyroid may be improved.

Treatment

The alcoholic is most often seen by the physician at the termination of a prolonged bout of drinking. He is usually in an extremely toxic condition, dehydrated, and may or may not be in a state of delirium. The immediate problem is the restoration of the patient to as near a physiologically normal state as is possible by the correction of his dietary deficiencies and dehydration and to substitute another medicament for the depressing drug, alcohol, which he can no longer tolerate.

There are two reasons for immediately discontinuing alcohol in such a patient; the first being the toxic effect of this substance on his already damaged liver and second the increased psychological dependence on the drug from its medical use.

The patient as first seen is a pitiful sight. It is at this point that the physician must exert all possible control over himself to avoid an instinctive feeling of superiority over the patient. This is probably the greatest barrier to successful treatment

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of an alcoholic patient and is one which is unconsciously assumed by the physician at the first visit. The patient is frightened, depressed, weak, restless, and unable to sleep. He has a tremor made worse by intention. The problem of hallucinosis and delirium tremens may also be present. On physical examination, he shows some increase in tendon reflexes and clonus may be observed. The pulse rate is increased and systolic and diastolic blood pressure may be elevated. There is a warm skin with some peripheral vasodilatation, and body temperature may be 99 F (37.2 C) or 100 F (37.8 C). The evidence of dehydration is present, as the diuretic action of alcohol has been active. The mouth is dry, the eyes are sunken, and the skin is wrinkled. Hematocrit values of 40 to 50% may be present, and this usually reflects a hemoconcentration without electrolyte disturbance. The alcoholic after a binge is usually starving as well, since most have lost weight and have nausea, vomiting, and diarrhea.

The correction of these physiological abnormalities is basically the responsibility of the family physician, and can and should be accomplished in the community general hospital. Fluid restoration is the primary aim, and 1,000 cc. of 5% dextrose in physiological saline solution followed by 1,000 cc. of 10% dextrose in distilled water should be given, together with parenteral administration of vitamin B complex and vitamin C, in the first two hours. Chlorpromazine (Thorazine) hydrochloride or promazine (Sparine) hydrochloride should be given intramuscularly at the onset and repeated in three or four hours. Subsequently, this should be given by mouth in divided doses. Mephobarbital (Mebaral) should be given by mouth concurrently. As soon as the nausea and vomiting have subsided, orally given fluids should be offered at frequent intervals, and food should be added as soon as it can be tolerated. Godfrey[4a] reports that on this regimen the hallucinations are gone and that convulsions no longer occur within 24 hours. He further states that on this regimen no patient has developed delirium tremens. Should this condition supervene, the continued administration of the above drugs and fluids is indicated, and on occasion it may be necessary to use corticotropin in doses of 25 mg. parenterally every four to six hours. In general, the other complications will subside with this method unless, for example, the gastritis is further complicated by bleeding esophageal varices, in which case a mechanical approach to the source of blood loss must be made.

In caring for the alcoholic after he regains sobriety, the family physician has a tremendous responsibility. He must treat a patient who does not admit his own disease and who usually shows little or no motivation for maintenance of the sober state. Rehabilitation can be accomplished if the physician is quick to sense the prodromal signs of an oncoming bout and, above all, if he, by his own attitude, can show the patient that he believes this is an illness worthy of continuing medical care and does not allow any personal prejudice against the "stigma" of alcoholism to be demonstrated. The use of drugs in the maintenance of the sober state is usually limited to larger medical centers, since the conditioned reflex type of withdrawal therapy needs occasional reinforcement. The use of disulfiram (Antabuse) has a definite place in effective withdrawal in certain persons and in certain institutions, but this requires the cooperation of the patient to the extent that he must take the medicament daily. If he loses the desire to do this, within 72 hours the drug will have been excreted, and he is then free to drink alcohol without physiological consequences.

Perhaps the single most effective force is the psychotherapeutic one, which offers the alcoholic many facets of refuge. The understanding physician who can treat and not reproach; the understanding wife and family who can accept the patient without reprehension; the community which can do likewise; and, above all, the local chapter of Alcoholics Anonymous are all a part of effective rehabilitation.

Summary

The medical management of the chronic alcoholic involves a knowledge of the effects of long-term consumption of alcoholic beverages, including the metabolic pathways involved. The rehabilitation of an alcoholic patient is long and tedious, since it involves an illness which has been present for some time and one in which motivation for recovery is poor. The family physician in the home community is best equipped to accomplish this rehabilitation.

P. O. Box 841 (Dr. Pannill).

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DETECTION OF HEPATITIS CARRIERS BY SERUM GLUTAMIC OXALACETIC TRANSAMINASE ACTIVITY

Nils U. Bang, M.D., Paul Ruegsegger, M.D., Allyn B. Ley, M.D.
and
John S. LaDue, M.D., Ph.D., New York

The prevention of homologous serum hepatitis (HSH) after transfusions depends on improved methods of detecting latent hepatitis among prospective donors. In a series of 1,371 recipients adequately followed up, 39 developed HSH. When the donor bloods were classified according to their serum glutamic oxalacetic acid transaminase (SGO-T) values, it was found that the incidence of HSH was only 1.5% among recipients of blood with normal SGO-T values while the corresponding figure was 5.5% for SGO-T values above 100 units. Since the differences were statistically significant, it appeared that SGO-T determinations would be more useful than most or all of the tests currently used for screening out hepatitis carriers among prospective blood donors.

The reported incidence of homologous serum hepatitis subsequent to blood transfussion is 0.3 to 1.9% in civilian hospitals [1] but was as high as 3.6% in soldiers given blood transfusions in the Korean theater of war.[2] By contrast, infectious hepatitis has a reported incidence of about 0.02%.[1b] An estimated 5 million transfusions are given in the United States each year,[3] and, although the total incidence of homologous serum hepatitis is not precisely known, on the basis of the above reports 15,000 to 100,000 cases of homologous serum hepatitis can be expected to develop each year. These patients are, as a rule, out of work for an average of six weeks and 1 to 5% will die.[4]

The precaution of refusing blood donations from persons who have a history of jaundice or of a recent upper respiratory infection cannot be expected to decrease significantly the occurrence of homologous serum hepatitis, since donors may be asymptomatic during the incubation period of hepatitis or may be infected with a subclinical or anicteric form of the disease.

The incidence of hepatitis carriers among the general population has been estimated to be 0.5 to 6%.[5] No specific bacteriological, immunological, or laboratory methods have yet been developed which will detect the presence of the virus of infectious hepatitis among blood donors. Determinations of thymol turbidity, cephalin flocculation reaction, urobilinogen level, zinc turbidity, and sulfobromophthalein (Bromsulphalein) retention have proved ineffective for screening hepatitis carriers.[6] This is not suprising, since the results of these tests are far from specific and may frequently be within normal limits during the incubation period of infectious hepatitis or in patients with subclinical or anicteric viral hepatitis.

The activity of the enzymes serum glutamic oxalacetic acid transaminase (SGO-T) and serum glutamic pyruvic acid transaminase increases early and significantly in both homologous serum hepatitis and infectious hepatitis. For example, inmates in a closed institution who were exposed to infectious hepatitis were found to have increased enzyme activity for a few days to 12 weeks before the onset of jaundice. Furthermore, only those inmates whose SGO-T level became elevated subsequently developed hepatitis.[7]

If, as appears likely from the above findings, an increase in SGO-T activity is the first evidence of impending infectious hepatitis, it can be assumed that increased enzyme activity in donors might be a useful screening test to eliminate hepatitis carriers.

From the Medical Service and the Blood Bank of the Memorial Center and the Sloan-Kettering Institute for Cancer Research.

of an alcoholic patient and is one which is unconsciously assumed by the physician at the first visit. The patient is frightened, depressed, weak, restless, and unable to sleep. He has a tremor made worse by intention. The problem of hallucinosis and delirium tremens may also be present. On physical examination, he shows some increase in tendon reflexes and clonus may be observed. The pulse rate is increased and systolic and diastolic blood pressure may be elevated. There is a warm skin with some peripheral vasodilatation, and body temperature may be 99 F (37.2 C) or 100 F (37.8 C). The evidence of dehydration is present, as the diuretic action of alcohol has been active. The mouth is dry, the eyes are sunken, and the skin is wrinkled. Hematocrit values of 40 to 50% may be present, and this usually reflects a hemoconcentration without electrolyte disturbance. The alcoholic after a binge is usually starving as well, since most have lost weight and have nausea, vomiting, and diarrhea.

The correction of these physiological abnormalities is basically the responsibility of the family physician, and can and should be accomplished in the community general hospital. Fluid restoration is the primary aim, and 1,000 cc. of 5% dextrose in physiological saline solution followed by 1,000 cc. of 10% dextrose in distilled water should be given, together with parenteral administration of vitamin B complex and vitamin C, in the first two hours. Chlorpromazine (Thorazine) hydrochloride or promazine (Sparine) hydrochloride should be given intramuscularly at the onset and repeated in three or four hours. Subsequently, this should be given by mouth in divided doses. Mephobarbital (Mebaral) should be given by mouth concurrently. As soon as the nausea and vomiting have subsided, orally given fluids should be offered at frequent intervals, and food should be added as soon as it can be tolerated. Godfrey[4a] reports that on this regimen the hallucinations are gone and that convulsions no longer occur within 24 hours. He further states that on this regimen no patient has developed delirium tremens. Should this condition supervene, the continued administration of the above drugs and fluids is indicated, and on occasion it may be necessary to use corticotropin in doses of 25 mg. parenterally every four to six hours. In general, the other complications will subside with this method unless, for example, the gastritis is further complicated by bleeding esophageal varices, in which case a mechanical approach to the source of blood loss must be made.

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John S. LaDue, M.D., Ph.D., New York

The prevention of homologous serum hepatitis (HSH) after transfusions depends on improved methods of detecting latent hepatitis among prospective donors. In a series of 1,371 recipients adequately followed up, 39 developed HSH. When the donor bloods were classified according to their serum glutamic oxalacetic acid transaminase (SGO-T) values, it was found that the incidence of HSH was only 1.5% among recipients of blood with normal SGO-T values while the corresponding figure was 5.5% for SGO-T values above 100 units. Since the differences were statistically significant, it appeared that SGO-T determinations would be more useful than most or all of the tests currently used for screening out hepatitis carriers among prospective blood donors.

The reported incidence of homologous serum hepatitis subsequent to blood transfussion is 0.3 to 1.9% in civilian hospitals[1] but was as high as 3.6% in soldiers given blood transfusions in the Korean theater of war.[2] By contrast, infectious hepatitis has a reported incidence of about 0.02%.[10] An estimated 5 million transfusions are given in the United States each year,[3] and, although the total incidence of homologous serum hepatitis is not precisely known, on the basis of the above reports 15,000 to 100,000 cases of homologous serum hepatitis can be expected to develop each year. These patients are, as a rule, out of work for an average of six weeks and 1 to 5% will die.[4]

The precaution of refusing blood donations from persons who have a history of jaundice or of a recent upper respiratory infection cannot be expected to decrease significantly the occurrence of homologous serum hepatitis, since donors may be asymptomatic during the incubation period of hepatitis or may be infected with a subclinical or anicteric form of the disease.

The incidence of hepatitis carriers among the general population has been estimated to be 0.5 to 6%.[5] No specific bacteriological, immunological, or laboratory methods have yet been developed which will detect the presence of the virus of infectious hepatitis among blood donors. Determinations of thymol turbidity, cephalin flocculation reaction, urobilinogen level, zinc turbidity, and sulfobromophthalein (Bromsulphalein) retention have proved ineffective for screening hepatitis carriers.[6] This is not suprising, since the results of these tests are far from specific and may frequently be within normal limits during the incubation period of infectious hepatitis or in patients with subclinical or anicteric viral hepatitis.

The activity of the enzymes serum glutamic oxalacetic acid transaminase (SGO-T) and serum glutamic pyruvic acid transaminase increases early and significantly in both homologous serum hepatitis and infectious hepatitis. For example, inmates in a closed institution who were exposed to infectious hepatitis were found to have increased enzyme activity for a few days to 12 weeks before the onset of jaundice. Furthermore, only those inmates whose SGO-T level became elevated subsequently developed hepatitis.[7]

If, as appears likely from the above findings, an increase in SGO-T activity is the first evidence of impending infectious hepatitis, it can be assumed that increased enzyme activity in donors might be a useful screening test to eliminate hepatitis carriers.

From the Medical Service and the Blood Bank of the Memorial Center and the Sloan-Kettering Institute for Cancer Research.

Materials and Methods

All donor bloods received in the blood bank of the Memorial Center between Dec. 20, 1955, and Jan. 1, 1957, a total of 14,296, were analyzed for SGO-T activity. The blood came from three different sources: a commercial blood bank, the Red Cross, and the Memorial Center blood bank. The latter blood was donated by friends and relatives of hospitalized patients. When possible, the bloods were tested one to seven days after they were received. In case of accumulation due to excessive in-[illegible] the serums were refrigerated and then tested [illegible] later date.

TABLE 1.—*Incidence of Abnormal SGO-T Activity in Blood from Various Sources*

Source	No. of Donor Bloods Tested	SGO-T <40 Units No	SGO-T <40 Units %	SGO-T,41-50 Units No.	SGO-T,41-50 Units %	SGO-T,51-100 Units No.	SGO-T,51-100 Units %	SGO-T>100 Units No.	SGO-T>100 Units %
Commercial blood bank	7,385	1,639	22.2	613	8.3	841	11.4	182	2.5
Memorial Center	2,142	265	12.4	102	4.8	137	6.4	26	1.2
Red Cross	3,739	1,178	31.5	418	11.1	648	18.3	76	2.0
Total tested	13,266	3,082	23.2	1,133	8.5	1,665	12.5	284	2.1
Not tested	1,030								

SGO-T activity was determined spectrophotometrically[8]; 40 units was considered the upper limit of normal. When hemolysis was visible but slight, values below 50 were considered normal. When excessive hemolysis was found, the blood was considered unsuitable for enzyme determination and therefore discarded for the purposes of this study.

Our facilities were insufficient for a follow-up of all of the 4,240 recipients of the 13,266 bloods tested. Of these recipients 2,857 were followed up either in our outpatient service or at home. In the latter instance information was obtained from post cards sent regularly for the first seven months after the patients had received their last blood transfusions. Patients who died within the first three months after receiving their last blood transfusion were not included in this study. None of these patients developed unequivocal hepatitis before death, and, while they might or might not have developed the disease if they had lived long enough, they could not be included in the statistical evaluation. The total number of patients who died within three months was 862, leaving 1,995 recipients for study. Of these 1,995 patients, 624 failed to answer the post cards. Adequate information for the six-month period after transfusion was thus available in 1,371 cases.

Blood transfusions were given to the patients before the results of the SGO-T determinations were known, so that two groups of recipients were formed: (1) a group numbering 603 that received only "normal blood" and (2) 768 recipients of one or more transfusions of "abnormal blood." However, patients in the latter group may or may not have received one or more normal transfusions. Some patients who developed jaundice were admitted to the Memorial Center for further study of the cause of jaundice; others were treated by their own physicians, who supplied the pertinent clinical and laboratory data to us. In the latter group it was often, but not always, possible to obtain serum for enzyme analysis and liver function studies.

All patients with hepatitis who had received blood transfusions during any previous admissions to other hospitals within the last year were excluded from the tabulation. The only patients included were those in whom the symptoms, signs, and course of the disease, as well as the result of the biochemical tests of liver function and enzyme studies, were characteristic of hepatitis. Patients in whom other diseases of the liver were suspected as the cause of jaundice were excluded.

Results

Table 1 shows the percentage of abnormal donor bloods from the commercial blood bank, the Memorial Center, and the Red Cross separated into ranges of SGO-T activity of from 41 to 50 units, 51 to 100 units, and above 100 units respectively. The donors from the commercial and Red Cross blood banks had approximately twice the incidence of elevated SGO-T activity of the donors from the Memorial Center blood bank. Although most elevations of SGO-T fell between 41 and 100 units, more than 2% of all donors tested showed highly abnormal values of more than 100 units. The incidence of abnormal values among the commercial and Red Cross donors was again found to be about twice as high as among donors from the Memorial Center.

The over-all incidence of abnormal values of SGO-T activity among 13,266 donor bloods tested reached an unexpected high of 23.2%. In this large series of apparently normal persons, it was found that nearly one out of four had SGO-T activity exceeding the generally accepted upper limit of normal of 40 units. This high incidence of abnormal SGO-T activity among the blood donors was, in part, due to the manner of handling the blood samples sent to the laboratory. Bloods from the Red Cross and commercial source had pilot tubes containing both blood cells and serum, unseparated, up to two to three weeks before being used. The bloods drawn from the Memorial Center were almost always promptly processed so that blood cells and serum were separated within one to three days.

TABLE 2.—*Variations in SGO-T Activity with Delayed Separation of Serum and Red Blood Cells in Donated Bloods*

SGO-T Units	Group 1 (100 Bloods) Immediately Separated	Group 2 (50 Bloods) First Analysis After 5 Min., No.	Group 2 (50 Bloods) Second Analysis After 2 Wk., No.
40	92	43	27
41-50	2	1	8
51-100	5	5	12
>100	1	1	3
Abnormal SGO-T*	8%	14%	46%

* Forty units considered upper limit of normal; when hemolysis visible but slight, values below 50 considered normal.

The following experiment demonstrates the effect of delayed separation of serum and red blood cells upon the level of SGO-T activity. SGO-T activity was determined in 150 donor bloods immediately after withdrawal. The blood cells and serum were separated immediately in 100 bloods (group 1), while aliquots of serum were withdrawn and analyzed after contact with red blood cells for five minutes and again after two weeks for 50 bloods (group 2). Table 2 shows the results of this experiment. When analyzed immediately after withdrawal, abnormal SGO-T levels were found in 9.3% of the entire group of 150 bloods. Fourteen per cent of the 50 bloods tested twice showed abnormal SGO-T levels on the first analysis immediately after withdrawal. On the second analysis, 23 (46%) of these serums, after two weeks' contact with the red blood cells at 4 C, showed an SGO-T level exceeding the upper limit of normal of 40 units. In 49 of the 50 samples the SGO-T activity was seen to increase from the first to the second test two weeks later. The increment in SGO-T activity after standing averaged 39.7% for the whole group.

The total number of cases of hepatitis in the 1,371 recipients studied for six months was 39. Nineteen of these were followed up at the Memorial Center while 20 were treated either by their own physicians or in other hospitals. The incubation period was less than six weeks in 9 and more than six weeks in 30 patients. In table 3 the number of cases of hepatitis developing within and after an incubation period of six weeks is expressed in percentages of the total number in each of three groups of recipients: (1) those given transfusions with an SGO-T level below 41 units; (2) those receiving one or more bloods with a level of activity between 41 and 100 units; and (3) those given one or more transfusions with an SGO-T level above 100 units. The total incidence of hepatitis in the group that had received blood with a level of SGO-T above 40 units is twice as high as in the group that received blood with normal SGO-T activity. In the group that received blood with an SGO-T level above 100 units, the incidence of hepatitis was three times as high as in the group that received only normal blood. When the cases with an incubation period of less than six weeks are subtracted, the percentages are found to be 1% for the group that received normal blood, 3.1% for the total group receiving abnormal blood, and 4.2% for recipients of blood with more than 100 units of SGO-T activity. The difference for both groups is statistically significant, with probability factors of 0.05 and 0.03 respectively.

TABLE 3.—*Incidence of Hepatitis in Recipients of Tested Donor Bloods*

Total No. of Recipients	SGO-T <41 Units		SGO-T 41-99 Units		SGO-T >100 Units		Total No. of Bloods with Abnormal SGO-T Activity	
	No.	%	No.	%	No.	%	No.	%
Cases of hepatitis	9	1.5	22	3.5	8	5.5	30	3.9
Incubation period more than 6 wk. ...	6	1	18	2.9	6	4.2	24	3.1
Incubation period less than 6 wk.	3	.5	4	.6	2	1.3	6	.8

Comment

The present data show that a significantly higher incidence of viral hepatitis is found among a group of recipients of blood with abnormal SGO-T activity than in a group that received blood with an SGO-T level of 40 units or less. The unexpected finding of a 23% incidence of abnormal SGO-T activity among the tested blood donors is partly an artifact which, statistically, does not materially weaken the significance of the results.

TABLE 4.—*Probability of Contracting Hepatitis from Blood Transfusions with Various SGO-T Levels*

	No. of Transfusions Administered					
Recipients	SGO-T	<40 Units	41-100 Units	>100 Units	Hepatitis Frequency	Best Estimate of Probability
Group 1 ..	1,391		0	0	8/1,391	0.0058
Group 2 ..	851		1,084	0	19/1,935	0.0098 p SGO-T 41-100: 0.0130*
Group 3 ..		339		128	6/467	0.0128 p SGO-T >100: 0.0209†

[*] Probability of contracting hepatitis from one transfusion with SGO-T activity 41-100. Calculation: 851 at p 0.0058——4.94 cases of hepatitis. Balance: 14.06/1,084—p: 0.0130.

[†] Probability of contracting hepatitis from one transfusion with SGO-T activity of >100 units. Calculation: 339 at p 0.0098——3.32 cases of hepatitis. Balance: 2.68/128—p: 0.0209.

The experiments performed after completion of the study demonstrated an over-all incidence of abnormal SGO-T activity of 9.3% among 150 bloods tested immediately after withdrawal, as compared with 46% in 50 serums left in contact with the red blood cells for 5 to 21 days before testing. The first percentage is of the same magnitude as that found among the donors of the Memorial Center blood bank, while the second figure approximates more closely that found among bloods received from the commercial and the Red Cross blood banks.

The group of recipients followed up in this series is not ideal for study, since it is composed mainly of patients with neoplastic diseases undergoing major surgery, who received multiple injections and infusions of blood during their hospital stay. Difficulty in establishing a correct diagnosis and in eliminating epidemiologic mechanisms other than blood transfusions may, to a certain extent, weaken the conclusions of a study of this kind. Chance of contamination was minimized by the use of disposable needles, syringes, and infusion equipment. From the statistical viewpoint it is objectionable that the recipients studied usually received multiple blood transfusions and that normal and abnormal transfusions were given in varying numbers in all cases.

The data were, therefore, reanalyzed statistically; both the total number of transfusions and the ratios of bloods with SGO-T activities below 40, between 41 and 100, and above 100 units given to each recipient were taken into account. In this cal[illegible]n only patients receiving 1 to 10 transfusions [illegible]alyzed, so that the number of cases of hep[illegible]ken into account was reduced to 35. Table [illegible]narized the results of this analysis. The best [illegible]e of p, that is, the probability of getting hepa[illegible] from blood transfusions with various SGO-T [illegible]vels, was calculated for each of these three groups of recipients. Table 4 expresses in different terms that the probability of getting hepatitis exists for 1 out of 173 recipients given one blood transfusion with an SGO-T level of less than 40 units, 1 out of 77 persons receiving one transfusion with an SGO-T activity of 41 to 100 units, and 1 out of 47 persons receiving one transfusion with an SGO-T level greater than 100 units. The differences between these three groups are statistically significant.

The original purpose of the present study was to establish whether any consistent relationship exists between infectivity of viral hepatitis and elevated transaminase activity in the donor population. The results indicate that the SGO-T test is a more useful method for detecting silent carriers of hepatitis virus than other tests of liver function previously evaluated in this context. This is true irrespective of whether donors are at some stage of the incubation period of viral hepatitis or have asymptomatic, anicteric, or subclinical viral hepatitis. These latter difficulties and unpredictable variables do not permit us, on the basis of this study, to draw definite conclusions about the advisability of discarding bloods with abnormal SGO-T activity. However, it is felt that the present results warrant further studies to elucidate whether an abnormal SGO-T activity reflects the presence of hepatitis virus in donor bloods in a sufficiently high percentage of cases to advocate the determination of SGO-T activity as a standard screening measure to be used by the blood banks to minimize the occurrence of homologous serum hepatitis.

Summary

Thirteen thousand two hundred sixty-six donor bloods were tested for serum glutamic oxalacetic acid transaminase (SGO-T) activity in an effort to evaluate the importance of subclinical hepatitis or "the carrier state" in the production of homologous serum hepatitis in the recipients of these transfusions. The significant findings were as follows: 1. One thousand three hundred seventy-one recipients of blood transfusions were adequately followed up for six months, and 39 (2.8%) of these developed homologous serum hepatitis. 2. Six hundred three of these patients were given blood with normal SGO-T activity, and nine (1.5%) developed hepatitis. 3. Another six hundred twenty-four of the patients followed up were given blood with an SGO-T activity of 41 to 99 units, and 22 (3.5%) developed hepatitis. 4. One hundred forty-four of the recipients followed up got blood with an SGO-T activity above 100 units, with a subsequent 5.5% incidence of hepatitis. 5. If transfusions had been restricted to the administration of donor blood with a SGO-T activity of 40 units or less, 9 rather than 39 cases of hepatitis among the 1,371 recipients studied would have been found. 6. It was calculated that the incidence of hepatitis from one blood transfusion with an SGO-T activity of less than 40 units was 0.0058; for one transfusion with an SGO-T activity of 41 to 99 units 0.0130, and for one transfusion of blood with an SGO-T level of 100 or more units 0.0209. These differences are statistically significant.

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CLINICAL NOTES

FOREIGN BODY (DRINKING GLASS) IN THE RECTUM

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Foreign bodies in the rectum are frequently reported in the surgical literature. Objects are often inserted accidentally. At other times they are deliberately inserted, and the question as to what prompts persons to do this is a moot one. Frequently, these foreign bodies inserted through the anus are the result of prankish debauches and practical jokes. Sometimes they are inserted for the purpose of sexual deviation, and slip beyond the grasp of the user. Often they are inserted by the psychotic person with no actual or apparent intent or purpose.

Unless it can be established that the presence of a foreign body in the rectum is the result of an accidental insertion, it is frequently difficult to evoke a satisfactory history from these patients as to the reason for its presence. This is understandable, as embarrassment often inhibits them from revealing the reasons for their deliberate act and their consequent predicament.

Macht[1] reported the removal of a small beverage bottle from a patient's rectum. In reviewing the literature, he found such objects reported in the rectum as a snuff box, a whisky glass, a 30-cm. mortar pestle, a cold cream jar, a lemon, an apple, chicken bones, a glass tube, portions of a broom handle, and a frozen pig's tail. Glendon[2] removed a jelly glass from the rectum by laparotomy; Gillespie[3] removed a petrolatum (Vaseline) bottle, Pretty[4] removed an ink bottle, and Scamahorn[5] removed a flashlight, rectally. Kleitsch[6] reported a patient who, after giving himself an enema with a colon tube, with unsatisfactory results, used an umbrella handle to break up what he thought was a fecal impaction. He was then unable to remove either the umbrella handle or the colon tube, which had become firmly held in place by a rectal spasm. Kleitsch removed the umbrella handle by traction and the colon tube was then ejected spontaneously.

As a rule, rectal examination will detect foreign bodies in the rectum. Occasionally, however, the foreign bodies migrate into the sigmoid or high within the abdominal cavity and may be unrecognized during rectal examination. One of us and Martin[7] reported an unusual case of surgical removal of a 9-in. case knife from the sigmoid of a patient whose complaint on admittance was "knife-like" pain in the region of the umbilicus. Rectal examination of this patient was negative.

Methods of Removal

Numerous ingenious devices have been used to remove foreign bodies rectally. Ball[8] removed an antiseptic solution (Listerine) bottle by this method, with a loop made from a wire coat hanger. Light bulbs have been removed by use of two spoons, one on either side, as "forceps." Bacon[9] removed a glass by filling the open end with plaster and inserting forceps into the plaster for a handle. With the open end toward the peritoneal reflection, a hole was drilled into the base, thus giving a site to which to apply traction. McLean and Smathers[10] reported the removal of a glass by introduction of lubricated tongue blades between the mucosa and the glass, with division of the anus in the posterior midline. Others have described grasping a glass with rubber-shod forceps over gauze, so as not to fragment it.

Surgical removal of foreign bodies from the rectum by laparotomy, either by opening the colon or by directing the foreign body downward toward the anus, is necessary in some instances.

Mortality

The mortality in patients with foreign bodies in the rectum, removed either rectally or surgically, remained prohibitively high for some time prior to the introduction of drugs to cleanse the colon and antibiotics to prevent or overcome infection. While laparotomy alone results in a low mortality, it is, however, axiomatic that the morality is increased when the colon is opened for surgical removal of a foreign body. However, with the recent advances in chemotherapy and antibiotics, this potential has also been greatly diminished.

Nevertheless, occasional deaths are reported after removal of foreign bodies from the rectum, and in some patients death is due to various physiological complications unrelated to attempts at removal. For example, Holcombe[11] reported a patient who had used an uncovered tennis ball to replace hemorrhoids, the ball having been pushed through the rectum beyond reach. The patient died before

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operation for removal could be carried out. Postmortem examination three hours later revealed the abdomen to be full of fluid and fecal content. When removed, the ball was surrounded by omentum, indicating that it had been lying free in the abdominal cavity for some time. Death, according to Holcombe, was apparently due to a combination of distention and pressure necrosis leading to rupture.

We are reporting a case of a psychotic patient who was found on examination to have a sharp and jagged-edged drinking glass in the rectum. Because of the fact that there were no presenting symptoms and no specific complaints, except for the patient's claim of the presence of a glass in his rectum, which he insisted had been there for two years, it was thought that a report of the case would be of interest. Factors leading to surgical removal of the glass are described.

Report of a Case

A 37-year-old man was admitted to Cook County Hospital Oct. 16, 1958, with the complaint of a broken glass in the rectum. The patient was brought to the hospital by members of his family, who stated that he was psychotic. This was borne out by the fact that the patient himself, who spoke only broken Lithuanian, said very little and, when he did speak, was completely incoherent. He had no complaints other than the presence of the misplaced drinking glass.

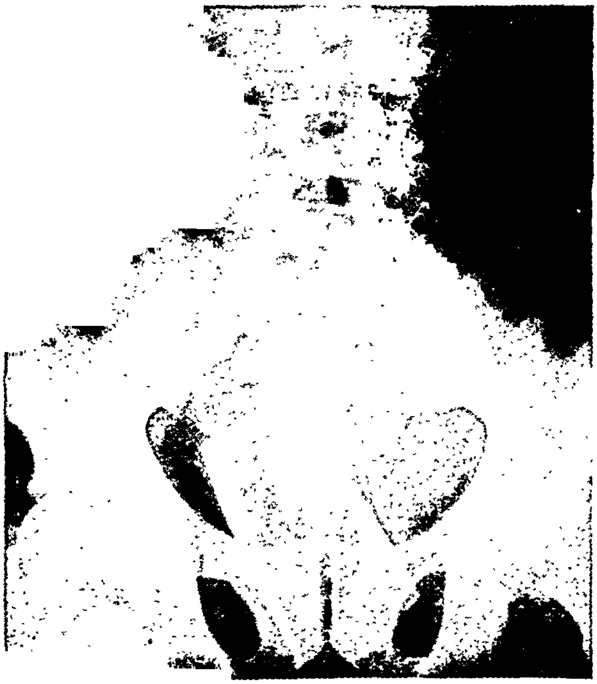

Fig. 1.—Position of drinking glass in rectum.

Physical examination revealed that the patient was well developed and was not in distress. Blood pressure was 140/90 mm. Hg, pulse 92 per minute, temperature 98.6 F (37 C), and respiration 16 minute. Rectal examination revealed a glass a tip of the examining finger. It was lying wit open end downward, and the edges were sharp jagged. The glass was filled with firm, impa feces. There was poor sphincter tone. A proctos was readily passed up to 12 cm. After clea and oil enemas were used to remove the impa feces, the proctoscope could be passed to the of the glass.

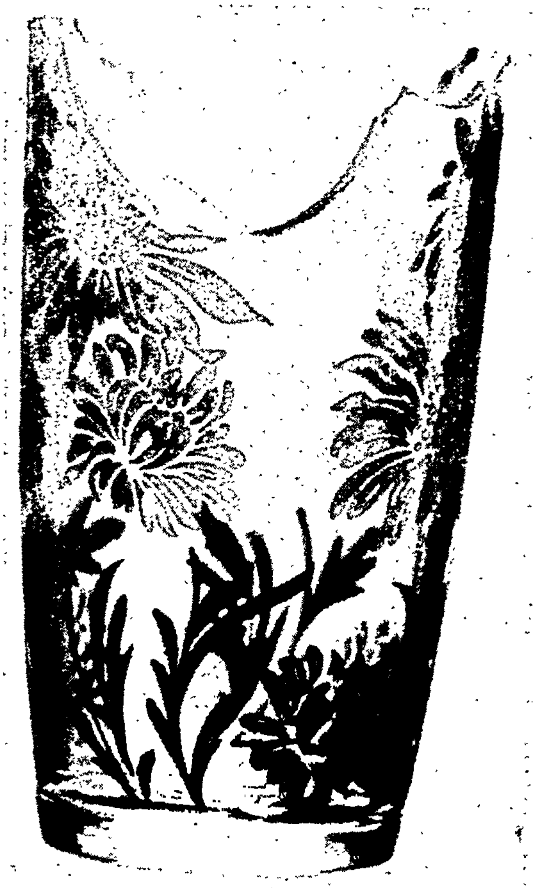

Fig. 2.—Jagged-edged drinking glass removed from re

On Oct. 18, 1958, with use of spinal anesth an attempt was made to remove the glass rect The open jagged edges of the glass engaged o sacral prominence and lacerated the mucosa. It evident that removal from below could no achieved without causing marked trauma to mucosa and sphincter. A roentgenogram was made, and revealed the position of the glass (fi

Surgery was decided on, and the patient given 2 Gm. of neomycin orally during the ne hours, and the intestine was cleansed with ene At operation a left paramedian incision was m the dilated rectosigmoid exposed, and a longit nal incision made. The glass was easily remo and the colotomy was closed transversely with chromic catgut and 0000 black silk. The peritoneum and anterior sheath were closed with one layer of no. 32 steel wire, and the skin was closed with fine wire. The glass is shown in figure 2. The patient's recovery was uneventful, and he was discharged on the ninth postoperative day.

Summary

A foreign body, in the form of a sharp, jagged-edged drinking glass, lying open end downward, was found in the rectum of a psychotic patient. An attempt was made to recover the glass rectally. However, it was found advisable to remove the broken glass by laparotomy, rather than to traumatize the rectal mucosa and sphincter by rectal removal. Cleansing the colon with neomycin, and with enemas when possible, greatly diminishes the morbidity and mortality associated with laparotomy for removal of a foreign body in the rectum.

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PSYCHOTHERAPY OF AN INFANT WITH RUMINATION

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Insufficient attention is given to the observation that infants can have psychiatric disorders. The infant is emotionally responsive and can react within the limits of his expressive capabilities with anxiety. From birth, disturbed behavior may occur as a somatic disorder, arrest of motor and behavioral maturation, and regression. Since the range of behavior in an infant is limited as compared to older children and adults, psychiatric disturbances in infancy have a greater tendency to be expressed as somatic complaints. Moreover, the etiology and management are intimately related to the mother. For a long time, the infant continues to be helpless and dependent on his mother and he is very much a unit with her, reflecting her emotional reactions and disturbances. An emotionally stable mother serves her infant's needs better than does an emotionally disturbed mother. Psychiatric treatment of an infant must involve the mother as an integral part of the baby. When the mother cannot be involved directly in treatment, a mother-surrogate must be supplied, since an infant cannot progress without a mother-child interrelationship. The following case report demonstrates how psychiatric emphasis in the management of an infant with severe rumination was probably lifesaving.

The syndrome of rumination has been well described by several authors recently.[1] In brief, rumination is the active, voluntary return of swallowed food to the mouth. This food may be partially or completely reswallowed or expelled. In some instances, the rumination may lead to progressive malnutrition. It differs from regurgitation, which is more involuntary, in that purposeful, preliminary movements of the mouth and tongue occur, and, on successful completion, an expression of gratification appears in the face.

The age of onset varies from 5 weeks to 12 months.[2] There seems to be no race or sex predisposition. The severity is variable, with a mortality up to 20% reported in the past [3]; this figure is probably lower at present. An organic cause for this syndrome is usually not found, and recently the psychiatric aspects have been stressed.[4]

Child Psychiatry Fellow, Child Psychiatry Division, Department of Psychiatry (Dr. Stein), Chief Pediatric Resident, Department of Pediatrics (Dr. Rausen), and Attending Psychiatrist-in-Charge, Child Psychiatry Division, Department of Psychiatry (Dr. Blau), the Mount Sinai Hospital.

Report of a Case

History.—An 8-month-old boy was admitted to the pediatric service of the Mount Sinai Hospital on Nov. 14, 1958, because of malnutrition, inability to retain food, and a 1,000-Gm. (2¼-lb.) weight loss in the two months prior to admission. The mother's pregnancy had been complicated by mild toxemia during the last trimester. Birth had been by delivery at home at term, with no physician in attendance. The infant's birth weight was 3,400 Gm. (7½ lb.). For the first six months of life, growth and development were normal. He received vitamin supplementation and had begun on a schedule of immunization. At 6 months of age, with no prior feeding difficulties, he weighed slightly more than 7,000 Gm. (16 lb.). At this time, he was seen in the Mount Sinai pediatric clinic for a rash ascribed to orange-juice or pear-juice allergy. With elimination of these juices, substitution of a soybean milk for cow's milk, and local therapy, the rash gradually cleared during the next month. Shortly thereafter, the child began to regurgitate his feedings, in spite of a good appetite. This was not affected by his position; solids and liquids dribbled out of his mouth without force within a few minutes after feeding. He was seen twice during the next month; a hemogram revealed mild hypochromic microcytic anemia, and wrist x-rays showed no bone-age retardation or rickets. Anticholinergic and sedative medication before feedings failed to alter the pattern of regurgitation.

Physical Examination.—On admission, the infant was markedly wasted, appeared chronically ill, and had an unhappy expression. Temperature was normal, pulse 120 beats per minute, head circumference 17.5 in. (44 cm.), chest circumference 15.5 in. (39 cm.), length 25 in. (64 cm.), and crown-to-pubis length 16 in. (41 cm.); respirations were 30 per minute. There was general malnutrition and some shotty anterior and posterior cervical lymphadenopathy; otherwise, physical examination was within normal limits.

Laboratory Data.—A hemogram showed moderate hypochromic anemia, with normal white blood cell and differential counts. Results of a test with a sickle-cell preparation and urinalysis were normal. Skin tests to purified protein derivatives, serum electrolyte and blood urea nitrogen determinations, nose and throat cultures, and lumbar puncture were noncontributory. An electroencephalogram was within normal limits, as were skull and chest x-rays. A barium-meal examination revealed no abnormalities of deglutition, normal esophagus, no evidence of hiatal hernia, and no free regurgitation of barium into the esophagus in the head-down position; the stomach appeared normal, barium appeared in the proximal part of the jejunum within 15 minutes, and there was normal distribution in the small intestine.

Course in Hospital.—On a diet of whole cow's milk and rice cereal, the infant continued to regurgitate, and two days after admission intravenous therapy was started. After another two days of giving nothing by mouth, oral feedings were reinstituted and, for the first time, a diagnosis of rumination was considered. Observation revealed that the expulsion of food involved a reverse sucking movement with the tongue and lips shortly after eating, associated with a look of determination; this brought the food back to his mouth, and it then oozed out.

During the next few weeks, various regimens were attempted, including thickened feedings, phenobarbital by mouth and parenterally, chlorpromazine, dextro amphetamine sulfate, nasogastric feeding tube, and intravenous therapy in various combinations. All were without long-lasting success, so that by Dec. 28, 1958, the infant weighed 5,100 Gm. (11¼ lb.) (15% less than his weight on admission and almost 30% less than his weight two months prior to admission). During this period, values of serum electrolytes, blood urea nitrogen, and serum proteins remained within normal limits.

A month after the infant's admission, psychiatric evaluation was requested. The tentative diagnosis offered was infantile anxiety neurosis with depression and a psychophysiological reaction of rumination.

The Mother.—The mother was first interviewed in the presence of the pediatric house staff. She was obviously depressed. An attractive, moderately obese 21-year-old woman, she was disturbed about her baby's illness. The eldest of three girls, she had felt the least loved and had had a deprived childhood. Her parents had been dancers, and she had lived with an aunt until 3 years of age. At that time, the present patient's grandmother had an episode of acute melancholia, did not eat, had to be tube fed, and nearly died; she recovered but subsequently never was able to give adequate care to her children.

During adolescence and after her second pregnancy, the patient's mother became obese, probably secondary to depressive trends. After graduating from high school, the patient went to work. She dated considerably and at one time wanted to escape from home into military service. Instead, she married at age 18. She soon became disappointed in her husband's lack of education and inability to earn more from his factory work. The husband was a passive, compliant man, interested in his family, who reacted to his wife's nagging by staying away from home and occasionally drinking to excess.

In three years of marriage, she had three children. The eldest has rare asthmatic attacks, and fell, without significant injury, from a second-story window in August, 1958. Both he and the patient were described by the mother as being sensitive.

The third pregnancy was unwanted. She resented being burdened with three children at 21 years of age. Hoping that a persistent vaginal infection would lead to abortion, she had not attended a prenatal clinic. The baby was born uneventfully at home. She felt that people were talking about her having three children in such close order. Unhappy, and prone to cry easily, she managed to care for her children until about three months prior to the patient's hospitalization, when her depression and inactivity increased. She developed severe headaches, was unable to do her housework, and stayed in bed. She began to prop up the infant in bed and spent little time with him. Then the rumination began.

Psychotherapy.—The patient's psychiatric needs were discussed with the pediatric house staff, and some changes in emphasis in treatment were advised. The rumination was understood to be a perverse pattern, developing a relation to the infant's anxiety, sense of neglect, depression, and insecurity at being rejected. More attention and fondling were planned, particularly during feedings. The infant responded at first but soon regressed to persistent rumination, and he was again tube fed. A female volunteer was enlisted to spend a few hours daily with him, but this, too, proved insufficient. Various nurses were able to abort his rumination temporarily by several methods. One nurse would scold him and, although this occasionally stopped his ruminating, he more often would cry and then regurgitate. Another nurse would fondle him and coo to him, but as soon as she had to leave he would ruminate again. The patient seemed voracious in his emotional needs, and it seemed impossible for the regular ward staff to satisfy these needs.

On Dec. 30, a full-time special nurse was engaged to spend eight hours daily with the patient. It was felt that this baby might respond to constant holding, warmth, and attention from one person. Fortunately, the nurse obtained was capable of performing this task with awareness of its importance. She stayed with him for one month, during which time a remarkable change occurred. He gradually ceased to ruminate and went from 5,100 to 6,700 Gm. (11¼ to 14¾ lb.). At the same time, he became a more responsive, happy baby, vocalizing and laughing, and he paid more attention to people and his surroundings. Significantly, at the beginning of special nursing, when the nurse was off duty, there was increased rumination.

Concurrently, one of us (M. L. S.) spent several hours a week with the mother. When it was suggested that the infant's difficulty might have a psychiatric genesis, she felt personally accused and guilty. Indeed, when she visited her baby, he seemed more disturbed, would scream and cry, and ruminated when she fed him. The mother was obviously tense and distant with the baby. She reduced her visits, and, when her child did not improve, she seemed pleased because this showed that she was not at fault. She was not discouraged from staying away from the child, since it was felt she might be better able to stabilize her own feelings in this way.

In psychiatric interviews, she was allowed to ventilate her feelings, and an attempt was made to allay her guilt. Gradually she was able to discuss better handling of her son. A doll was used to aid in demonstrating better ways of holding the infant close to her and not just leaving him propped or on her lap. Despite her sense of anxiety and depression, she was assured that the child needed her. As she began to visit her son again, she would hold him on her lap dutifully but without any mutual response. Gradually she held him more closely. As her son began to smile when she visited, she responded, and, reciprocally, his improvement helped her. She learned also by observing the behavior and handling of the baby by the special nurse and gradually was able to function better as a mother.

Follow-up.—The infant was discharged on Feb. 3, 1959. Since it was felt that the mother was unable as yet to undertake full responsibility, a part-time homemaker was arranged for from a community agency. The mother continued in psychotherapy. The infant progressed well, regurgitated rarely, and gained weight progressively; he weighed 10,000 Gm. (22 lb.) two months after discharge (a gain of over 3,000 Gm. [7 lb.] in two months). He reacted normally to people around him and seemed happier. He played and laughed with his siblings and matured to a level commensurate with his chronological age.

Comment

Some illnesses in infancy are complicated by emotional factors in the family. Comprehensive care requires attention to these factors. In most cases, this level of psychiatric treatment rests with the pediatrician, with psychiatric consultation when necessary. Additional personnel may be necessary to assist in this avenue of treatment. We are attempting to develop a "mother bank" of volunteers who would be able, under supervision, to act as mother-surrogates when needed.

This case also demonstrates the need for maternal love, fondling, and attention for the well-being and normal development of an infant. Furthermore, evidence is accumulating that emotional trauma in infancy may be of critical significance in the development of later psychiatric disorders. Early treatment seems to be the keystone to the prevention of later serious disorders. The rumination seemed to be a physiological concomitant of anxiety and depression, coincident with a similar emotional disturbance in the mother. Separation of mother and infant by hospitalization was insufficient, because a pattern had already been established. The process was reversed by introducing a warm mother-surrogate. The mother received supportive psychiatric treatment, and, on the baby's discharge, a temporary homemaker was employed to help the mother make the transition to complete care by herself. The infant continued to improve and develop normally after discharge.

Summary

Psychotherapeutic management of both infant nd mother brought improvement in a case of tile rumination.

Fifth Avenue and 100th Street (29) (Dr. Blau).

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2. Reference 1*d* and *h*.
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RETROCAVAL URETER—UNUSUAL CAUSE OF URETERAL OBSTRUCTION

Clair E. Laidig, M.D.
and
James M. Pierce Jr., M.D., Detroit

The term retrocaval ureter is used interchangeably with circumcaval or postcaval ureter, which describes the anatomic relationship of the ureter to the embryologically abnormal inferior vena cava. The designation preureteric vena cava more accurately describes the embryologic malformation; however, this is not as practical a term because the functional abnormality is only manifest clinically by obstruction of the ureter.

A retrocaval ureter courses toward the midline on the posterior aspect of the inferior vena cava before emerging medial and anterior to this structure and then descending into the pelvis. It is nearly always single and located on the right side. Hydro- [illegible] and hydroureter above the postcaval obstruction [illegible] may develop if the vena cava [illegible] obstruction. When obstructed, [illegible] present [illegible] without hematuria. [illegible] with the ureteral

In 1893, Hochstetter[1] first described retrocaval ureter in man. He and others found the abnormality also present in sheep, rabbits, cats, and hedgehogs. An excellent study by McClure and Butler[2] first described the essential features of the embryologically abnormal inferior vena cava which produces the aberration.

In figure 1 the postcardinal, subcardinal, and supracardinal veins are seen to be the essential vascular elements which form a ureteral venous ring during the development of the infrarenal vena cava. Normally the infrarenal vena cava arises from the dorsal portion of this ring which is composed of the postcardinal, supracardinal, and subcardinal ins. If, however, the ventral segment of the r sists then a retrocaval ureter will exist. Th segment may persist with the posterior se produce a ring or alone as a p eteric v The preureteric vena cava is d from cardinal and subcardinal vein

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other hand, Pick and Anson[4] found one case in 570 anatomic dissections. The cadaver's ureter revealed no significant obstruction which would indicate the cause for the discrepancy in incidence.

Report of a Case

Our patient was a robust 37-year-old male who complained of increasing right flank distress for six months. The pain was not incapacitating but was associated with frequency, urgency, and nocturia one to four times. He denied other symptoms or history referable to the urinary tract. The physical examination together with the hematological and serologic specimens were within normal limits. The urine contained 1 to 2 white blood cells, 7 to 10 red blood cells, and an occasional bacillus per high-power field. In addition to a normal plasma urea nitrogen level, the 15-minute phenolsulfonphthalein test result was 20% and the creatinine clearance was 86 ml. per minute. The endoscopic and cystocopic examinations of the urethra and bladder revealed no abnormalities.

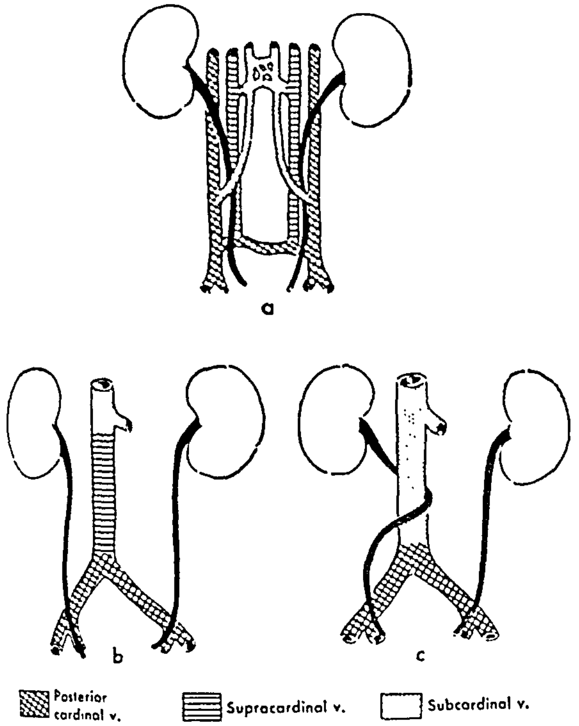

Fig. 1.—Embryology of infrarenal vena cava: *a*, bilateral ureteral venous rings normally present early in development of vena cava; *b*, normal adult vena cava; *c*, preureteric vena cava. (Reproduced, with permission, from Hollinshead, W. H.: Anatomy for Surgeons: II. Thorax, Abdomen, and Pelvis, New York, Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 1956, pp. 571-572.)

The intravenous urogram disclosed a normal left pyelogram and an abnormal right ureter and renal pelvis. More exactly, the bulb retrograde pyelogram in figure 2 describes the right ureter which has an s-shaped curve at the junction of the middle and upper portion, with dilatation of the upper portion and renal pelvis. Characteristically, the postcaval portion passes medially toward, or occasionally even across, the midline, forming a sigmoid curve with the convexity upward and medial.[4] In figure 3 the oblique pyelogram shows the postcaval segment of the ureter to extend medially with the distal curve coursing posterior to the more proximal ureter. While a normal ureter will fall away, anteriorly, from the vertebral column, the postcaval ureter lies against the bodies of the lower lumbar vertebra. Presman and Firfer[5] emphasized this finding in the roentgenographic diagnosis by recording simultaneously placed radiopaque catheters in the inferior vena cava and the retrocaval ureter.

Therapy

Therapy for the relief of the ureteral obstructing preureteric vena cava is surgical repositioning of the ureter anterior to the inferior vena cava. Four basic methods have been utilized in the repair of retrocaval ureters. These are (1) section and reanastomosis above the postcaval segment, (2) section near the postcaval segment with or without removal of a ureteral segment prior to reanastomosis, (3) section at the ureteral-vesical junction with reimplantation of the ureter into the bladder, and

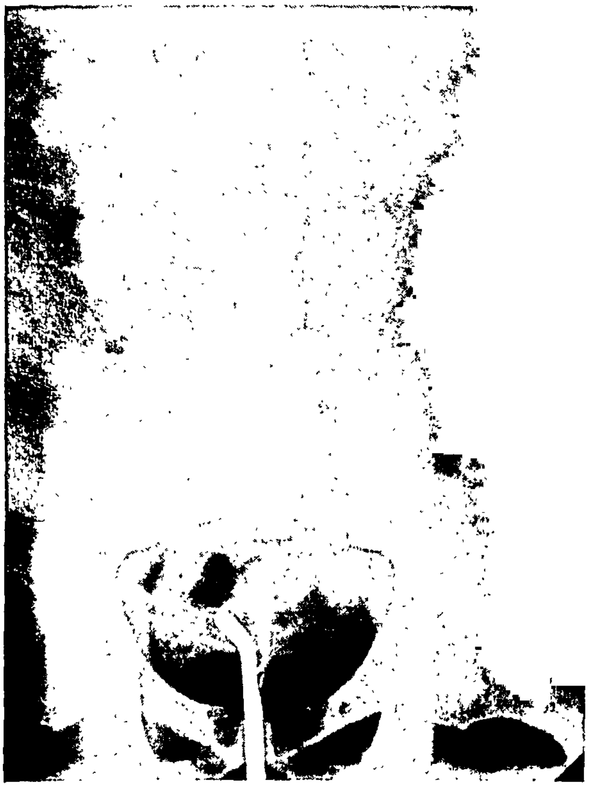

Fig. 2.—Preoperative right bulb retrograde pyelogram.

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In 1893, Hochstetter[1] first described retrocaval ureter in man. He and others found the abnormality also present in sheep, rabbits, cats, and hedgehogs. An excellent study by McClure and Butler[2] first described the essential features of the embryologically abnormal inferior vena cava which produces the aberration.

In figure 1 the postcardinal, subcardinal, and supracardinal veins are seen to be the essential vascular elements which form a ureteral venous ring during the development of the infrarenal vena cava. Normally the infrarenal vena cava arises from the dorsal portion of this ring which is composed of the postcardinal, supracardinal, and subcardinal veins. If, however, the ventral segment of the ring persists then a retrocaval ureter will exist. The ventral segment may persist with the posterior segment to produce a ring or alone as a preureteric vena cava. The preureteric vena cava is derived from the postcardinal and subcardinal veins.

The literature contains reports of 59 patients with retrocaval ureter and of these only 22 were treated surgically. Abeshouse[3] reported only one case in 120,000 general hospital admissions. On the

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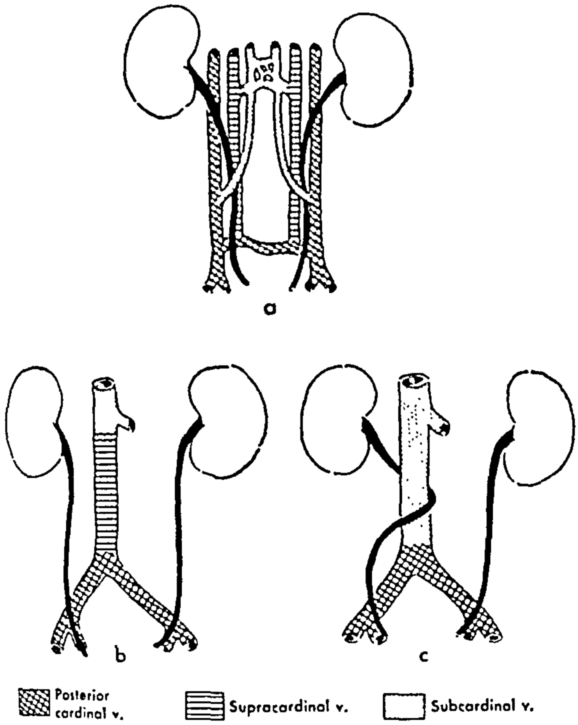

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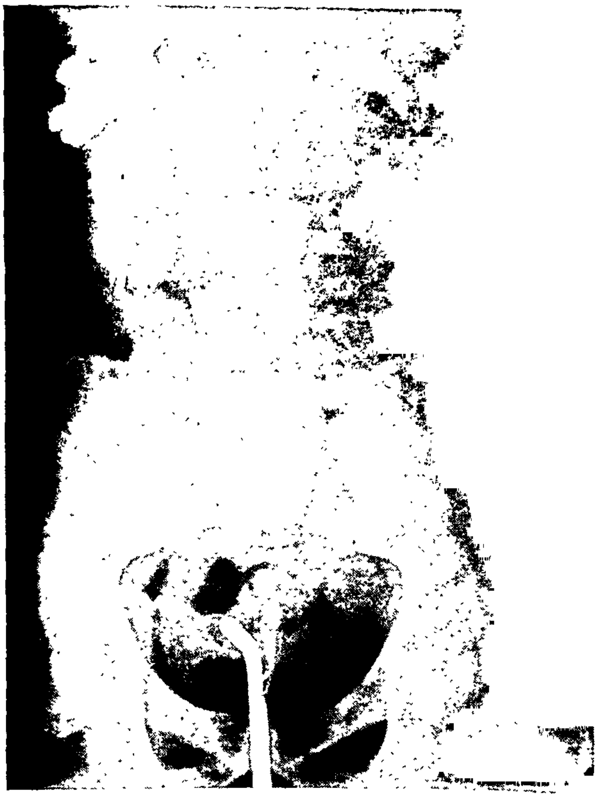

Fig. 2.—Preoperative right bulb retrograde pyelogram.

Therapy

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(4) section of the inferior vena cava without incision into the ureter. Although Abeshouse,[3] who reviewed the surgical treatment of 22 patients, believed that each patient must be treated individually, section above the postcaval segment generally gave the best results. Only one patient with inferior vena cava section was reported and the result of surgery was good. Further work may prove the latter procedure valuable; however, the inherent possible complications of such a procedure did not, in our opinion, justify its use in our patient.

Our patient's right ureter was freed bluntly from the infrarenal vena cava, sectioned in the upper dilated portion, and drawn anterior to the vena cava. Here, it was examined closely to be certain that the postcaval segment was normal before the lower segment was spatulated and the equal ureteral openings approximated without a splinting catheter. The postoperative period was uneventful and the flank drainage stopped on the 13th day after operation.

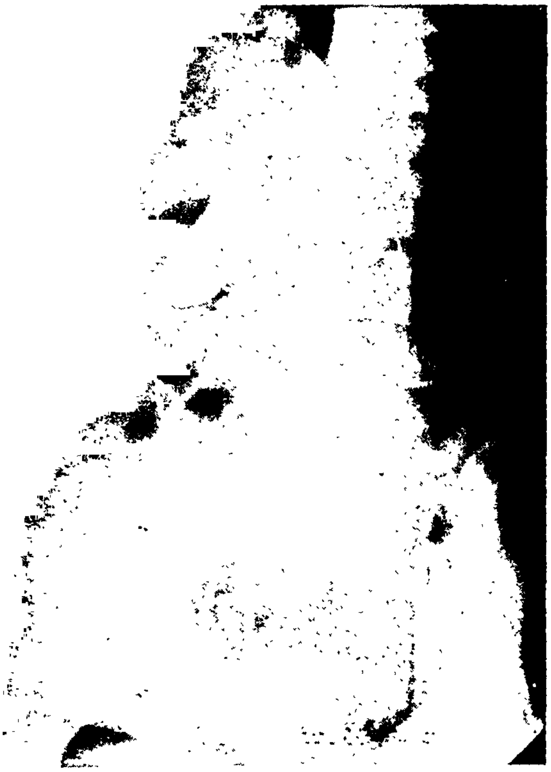

Fig. 3.—Preoperative right oblique bulb retrograde pyelogram.

The intravenous pyelogram taken six weeks after operation (fig. 4) showed prompt function with no alteration in the upper portion of the ureter or pelvic dilatation. Initially after operation his urine contained numerous white blood cells and bacilli; however, on discharge from the hospital he was free of pain. After three months the urine showed no bacteria and only an occasional white blood cell. He is now asymptomatic and has resumed his job as a manual laborer.

Summary

A retrocaval ureter is an unusual cause of hydronephrosis which is produced by the embryologic malformation of the infrarenal vena cava. If recognized before the resultant hydronephrosis has destroyed the kidney, operative correction of the defect can prevent further damage to the kidney. Sectioning the dilated upper ureteral segment in order to gain proper ureteral positioning and wide-caliber reanastomosis without intubation proved to be a successful method for surgical correction of the retrocaval ureter.

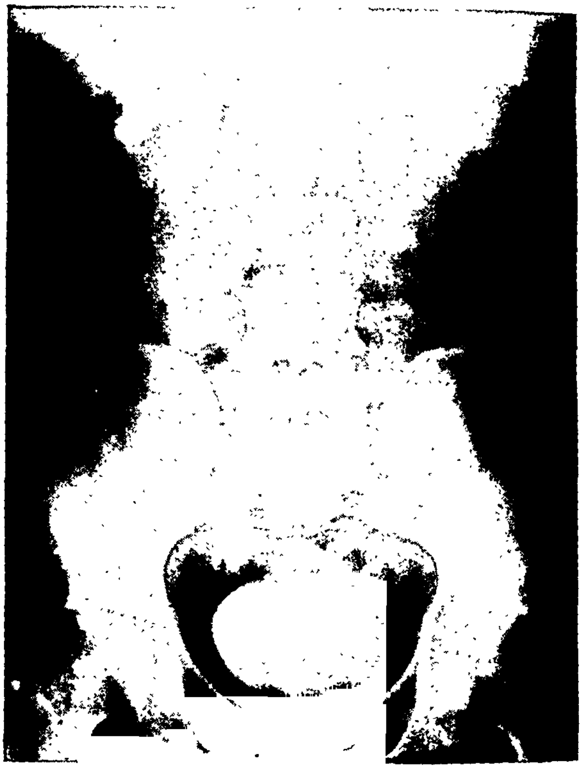

Fig. 4.—Intravenous urogram taken six weeks after operation.

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DEFICIENCY OF PROTHROMBIN AND PROCONVERTIN AFTER THERAPY WITH PROPYLTHIOURACIL

Charles P. Kolars, M.D.
and
Lorraine M. Gonyea, M.S., Minneapolis

Thiouracil and its derivatives have been implicated as the cause of a variety of toxic reactions, the most common of which are agranulocytosis, leukopenia, and drug fever; cases of hepatitis and thrombocytopenia have also been described.[1] Recently we have observed two patients in whom severe bleeding occurred after administration of propylthiouracil. Survey of the literature revealed only three cases in which disturbance of the clotting mechanism was reported after the use of propylthiouracil.[2] In these patients the defect was associated with a prolonged Quick prothrombin time and appeared to respond to administration of blood or serum. Observations on our two patients have suggested a similarity between this apparently rare reaction to propylthiouracil and the therapeutic response to bishydroxycoumarin (Dicumarol). Since this appears to be a serious but little-known complication of the use of the latter drug, it is hoped that presentation of results of studies done on our cases will be of value.

Report of a Case

A 60-year-old housewife was admitted to the University of Minnesota Hospitals on Aug. 2, 1957. She was referred because of the development of purpura, hematuria, and bleeding gums of three days' duration. These symptoms had appeared four weeks after the initiation of a course of propylthiouracil, 400 mg. daily, for a toxic nodular goiter. Goiter had been present since she was 16 years of age. The only other medicaments she had received in the recent past were penicillin orally administered for a viral pneumonitis and an unknown vitamin preparation.

She was first admitted to another hospital at the onset of symptoms. At that time, the patient's hemoglobin level was 9.9 Gm.%, the leukocyte count was 9,800 per cubic millimeter, platelets "appeared normal on smear," and the urine was grossly bloody. She was given 200 mg. of cortisone acetate intramuscularly and 1,000 ml. of whole blood. She was then transferred to the University Hospitals and admitted on the evening of Aug. 2, 1957, the third day of her illness.

There was no history of serious bleeding requiring treatment in the patient or in members of her family, although she felt that she, her mother, and a brother had always bruised easily. When she was 34 years old the patient had an abdominal cystic mass removed without hemorrhagic complications. The remainder of her history was not significant.

Physical examination revealed a blood pressure of 130/70 mm. Hg, a pulse rate of 88 per minute, and a normal temperature. The patient was thin and anxious, with a body weight of 87 lb. (39.5 kg.) and fine hair. There was no lid lag. A firm, enlarged nodular thyroid, over which no bruit could be heard, was noted. There was no lymphadenopathy and no hepatosplenomegaly. Neurological examination revealed quick, deep tendon reflexes without pathological reflexes. There was no tremor. The most striking physical finding consisted of ecchymotic areas over the arms, chest, and legs. Purpuric areas were noted on the buccal mucosa and the palate. Result of the Rumpel-Leede test was negative. The remainder of the physical examination was normal.

Laboratory data revealed a hemoglobin level of 13.8 Gm.%, a leukocyte count of 10,950 per cubic millimeter, and platelet counts of 156,000 and 200,000 per cubic millimeter on Aug. 2 and Aug. 3, 1957, respectively. The urine was amber in color and contained 1+ albumin and 3+ erythrocytes. The erythrocyte sedimentation rate (Westergren) was 63 mm. per hour. Liver function tests showed a sulfobromophthalein retention of 0%, an alkaline phosphatase level of 7.2 King-Armstrong units, a thymol turbidity of 1 unit, a cephalin-cholesterol flocculation value of 2+, and a cholesterol level of 122 mg.%. An x-ray of the chest was normal, and an electrocardiogram revealed a sinus tachycardia with a vertical heart. Subsequently, an x-ray film of the neck revealed several small irregular, calcified areas just above the thoracic inlet in the lower part of the neck, which were felt to represent calcifications within thyroid adenomas. The trachea was shown to deviate slightly to the right. Rate of radioactive iodine uptake was 16%, level of protein-bound iodine 8.3 mcg.%, and level of blood urea nitrogen 47 mg.%. Stool guaiac reaction was 2+. Bleeding time (Ivy) was 4 minutes, blood clotting time (capillary) 6 minutes 30 seconds, prothrombin time (Quick) 33.6 seconds (control 14.0), and clot retraction normal.

The patient was given 25 mg. of phytonadione (vitamin K_1 oxide, Mephyton) intravenously, and four hours later a similar dose was given. The following day, the prothrombin time was 19.8 seconds

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From the departments of medicine and medical technology, University of Minnesota.

(4) section of the inferior vena cava without incision into the ureter. Although Abeshouse,[3] who reviewed the surgical treatment of 22 patients, believed that each patient must be treated individually, section above the postcaval segment generally gave the best results. Only one patient with inferior vena cava section was reported and the result of surgery was good. Further work may prove the latter procedure valuable; however, the inherent possible complications of such a procedure did not, in our opinion, justify its use in our patient.

Our patient's right ureter was freed bluntly from the infrarenal vena cava, sectioned in the upper dilated portion, and drawn anterior to the vena cava. Here, it was examined closely to be certain that the postcaval segment was normal before the lower segment was spatulated and the equal ureteral openings approximated without a splinting catheter. The postoperative period was uneventful and the flank drainage stopped on the 13th day after operation.

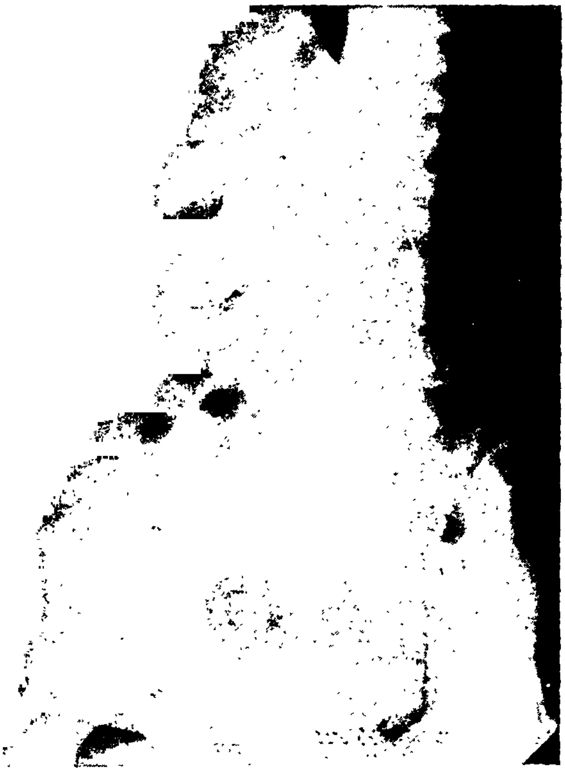

Fig. 3.—Preoperative right oblique bulb retrograde pyelogram.

The intravenous pyelogram taken six weeks after operation (fig. 4) showed prompt function with no alteration in the upper portion of the ureter or pelvic dilatation. Initially after operation his urine contained numerous white blood cells and bacilli; however, on discharge from the hospital he was free of pain. After three months the urine showed no bacteria and only an occasional white blood cell. He is now asymptomatic and has resumed his job as a manual laborer.

Summary

A retrocaval ureter is an unusual cause of hydronephrosis which is produced by the embryologic malformation of the infrarenal vena cava. If recognized before the resultant hydronephrosis has destroyed the kidney, operative correction of the defect can prevent further damage to the kidney. Sectioning the dilated upper ureteral segment in order to gain proper ureteral positioning and wide-caliber reanastomosis without intubation proved to be a successful method for surgical correction of the retrocaval ureter.

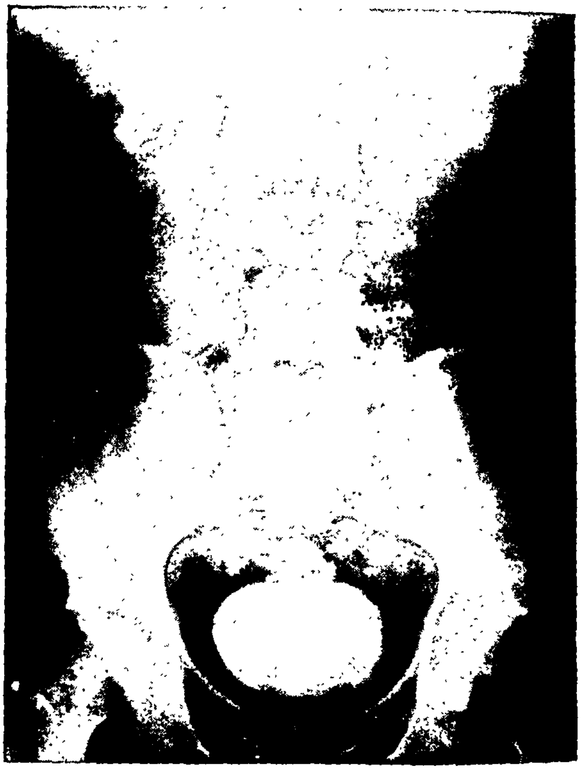

Fig. 4.—Intravenous urogram taken six weeks after operation.

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DEFICIENCY OF PROTHROMBIN AND PROCONVERTIN AFTER THERAPY WITH PROPYLTHIOURACIL

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and
Lorraine M. Gonyea, M.S., Minneapolis

Thiouracil and its derivatives have been implicated as the cause of a variety of toxic reactions, the most common of which are agranulocytosis, leukopenia, and drug fever; cases of hepatitis and thrombocytopenia have also been described.[1] Recently we have observed two patients in whom severe bleeding occurred after administration of propylthiouracil. Survey of the literature revealed only three cases in which disturbance of the clotting mechanism was reported after the use of propylthiouracil.[2] In these patients the defect was associated with a prolonged Quick prothrombin time and appeared to respond to administration of blood or serum. Observations on our two patients have suggested a similarity between this apparently rare reaction to propylthiouracil and the therapeutic response to bishydroxycoumarin (Dicumarol). Since this appears to be a serious but little-known complication of the use of the latter drug, it is hoped that presentation of results of studies done on our cases will be of value.

Report of a Case

A 60-year-old housewife was admitted to the University of Minnesota Hospitals on Aug. 2, 1957. She was referred because of the development of purpura, hematuria, and bleeding gums of three days' duration. These symptoms had appeared four weeks after the initiation of a course of propylthiouracil, 400 mg. daily, for a toxic nodular goiter. Goiter had been present since she was 16 years of age. The only other medicaments she had received in the recent past were penicillin orally administered for a viral pneumonitis and an unknown vitamin preparation.

She was first admitted to another hospital at the onset of symptoms. At that time, the patient's hemoglobin level was 9.9 Gm.%, the leukocyte count was 9,800 per cubic millimeter, platelets "appeared normal on smear," and the urine was grossly bloody. She was given 200 mg. of cortisone acetate intramuscularly and 1,000 ml. of whole blood. She was then transferred to the University Hospitals and admitted on the evening of Aug. 2, 1957, the third day of her illness.

There was no history of serious bleeding requiring treatment in the patient or in members of her family, although she felt that she, her mother, and a brother had always bruised easily. When she was 34 years old the patient had an abdominal cystic mass removed without hemorrhagic complications. The remainder of her history was not significant.

Physical examination revealed a blood pressure of 130/70 mm. Hg, a pulse rate of 88 per minute, and a normal temperature. The patient was thin and anxious, with a body weight of 87 lb. (39.5 kg.) and fine hair. There was no lid lag. A firm, enlarged nodular thyroid, over which no bruit could be heard, was noted. There was no lymphadenopathy and no hepatosplenomegaly. Neurological examination revealed quick, deep tendon reflexes without pathological reflexes. There was no tremor. The most striking physical finding consisted of ecchymotic areas over the arms, chest, and legs. Purpuric areas were noted on the buccal mucosa and the palate. Result of the Rumpel-Leede test was negative. The remainder of the physical examination was normal.

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(control 14.8). Between Aug. 2 and Sept. 1, 1957, although no further bleeding occurred, repeated doses of phytonadione were necessary to control the level of the prothrombin. The blood urea nitrogen level was 21 mg.% on Aug. 8. Requirements of phytonadione and fluctuations in the prothrombin time are shown in figure 1.

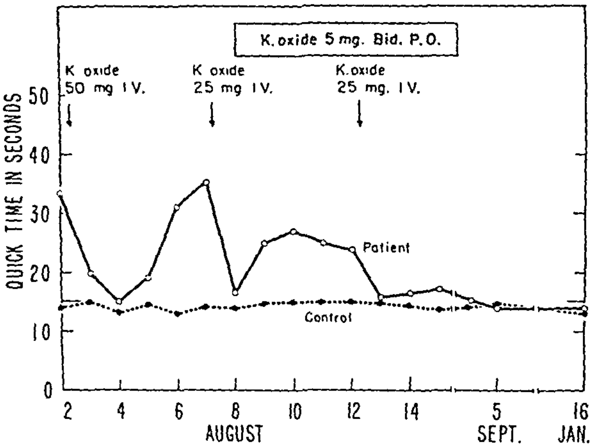

Fig. 1.—Response to phytonadione as measured by Quick prothrombin time.

The patient was discharged on Aug. 15, 1957, on a regimen of a daily, oral dose of phytonadione, which was discontinued on Sept. 1, 1957. Three weeks after discharge, the Quick prothrombin time was 13.9 seconds. She was seen again after four months, at which time the prothrombin time was 13.7 seconds. She had gained 20 lb. (9.1 kg.) in body weight since discharge from the hospital and was completely asymptomatic, with a hemoglobin level of 15.6 Gm.%, and a protein-bound iodine level of 6.4 mcg.%. She was clinically euthyroid.

Quick Method Prothrombin Times, per Milliliter—Mixtures of Patient's Plasma and Known Plasmas

Patient's, Plasma	Saline	Normal Plasma	Normal Adsorbed Plasma	Normal Serum	Proconvertin-Deficient Plasma	Stuart Factor-Deficient Plasma	Prothrombin Time, Sec.	Correction
0.1							18.4	
0.05	0.05						23.5	
		0.1					13.8	
	0.05	0.05					15.6	
0.05		0.05					14.5	+
0.08		0.02					14.5	+
0.05			0.05				24.0	0
0.05				0.05			12.0	+
0.05					0.05		25.4	0
0.05						0.05	13.2	+

Experiments with Prothrombin and Proconvertin Activity

In order to define the deficiency made apparent by the prolonged Quick prothrombin time, two experiments were conducted during our patient's period of hospitalization. These studies were confined to the aspect of coagulation measured by the Quick prothrombin system.

Experiment 1.—Mixtures of the patient's plasma with normal plasma, normal barium sulfate–adsorbed plasma, normal serum, and plasmas deficient in proconvertin (factor VII), and in Stuart factor were measured by the Quick system. Results obtained from these mixtures are shown in the table. Correction of the patient's prolonged Quick prothrombin time occurred with normal plasma, normal serum, and plasma deficient in Stuart factor. No correction occurred with barium sulfate–adsorbed plasma, nor with plasma deficient in proconvertin. These results indicate that the defect was (1) probably not due to the presence of a circulating anticoagulant; (2) not due to a lack of fibrinogen (factor I), proaccelerin (factor V), or the Stuart factor; and (3) corrected when plasma or serum containing prothrombin and/or proconvertin was added to patient's plasma.

Experiment 2.—The combined activity of prothrombin and proconvertin was measured by the method of Owren and Aas.[3] Prothrombin was measured by the specific one-stage method of Hjort and co-workers,[4] with use of Russell's viper venom and cephalin as thromboplastin. Results are shown in figure 2. When the prothrombin method of Hjort was altered to eliminate the effect of the Stuart factor,[5] identical results were obtained. The prothrombin–proconvertin concentration, which decreased to less than 10% even after institution of phytonadione therapy, did not respond until the sixth day after a total of 75 mg. of phytonadione had been administered. The concentration of prothrombin, which decreased to 15%, appeared to return toward normal more slowly. After four months, normal levels were found in both test systems.

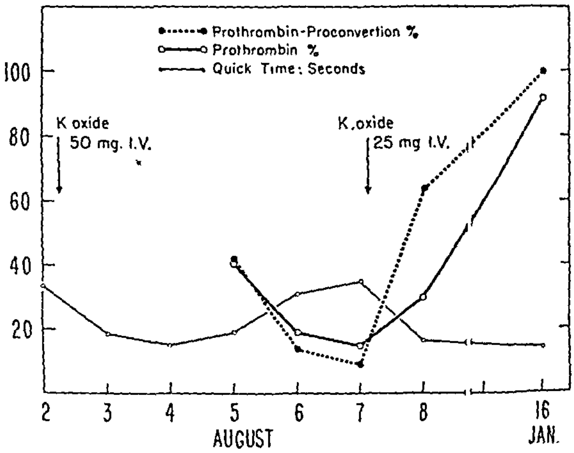

Fig. 2.—Response to phytonadione: comparison of Quick prothrombin method and prothrombin-proconvertin method. Units on ordinate represent seconds (Quick time) and per cent activity (prothrombin-proconvertin method).

Venous clotting times (modification of Lee-White method), determined on Aug. 6, 1957, and on Jan.

16, 1958, were within the normal range of 14 to 20 minutes (15 minutes 30 seconds and 20 minutes respectively).

It was concluded that the patient had a dual deficiency of prothrombin and proconvertin.

A brother of the patient, referred to by her as showing easy bruisability, was found to have a normal Quick prothrombin time, normal prothrombin concentration, and normal prothrombin-proconvertin concentration.

Comment

Three cases of "hypoprothrombinemia" after propylthiouracil treatment have been described in the literature. Craddock and associates,[2a] in 1951, reported a 16-year-old girl who had received 300 mg. of propylthiouracil daily for a period of six months, at which time hospitalization was required for continuous bleeding from the nose and from an abrasion on her arm. Routine laboratory tests were all normal, including liver function tests, with the exception of the Quick prothrombin time which was 200 seconds (control 12). Bleeding was controlled with repeated injections of thrombin-free serum, and the prothrombin time returned to normal levels within five days. Craddock concluded that this patient had a deficiency of labile factor (proaccelerin), which he attributed to a toxic effect of the propylthiouracil.

A second case was reported by Miner in 1955.[2b] He described a 43-year-old woman who noted hematuria, hemoptysis, and excessive uterine bleeding after five months of propylthiouracil therapy. All studies were normal except for a blood coagulation time of 32 minutes and a Quick prothrombin time of 20 seconds (control 13). She was treated with a 5-ml. intravenous dose of phytonadione, cortisone, and infusion of one unit of blood. Dramatic improvement was noted. The prothrombin time returned to normal within 48 hours. After three months no evidence of recurrent bleeding appeared. Miner postulated that the whole-blood transfusion provided the plasma factor or the "labile factor" and concluded that this was the factor deficient in this patient's blood.

A third case was reported by Goldstein [2c] in 1951 and, although he did not implicate propylthiouracil as the precipitating agent, in the light of the cases subsequently reported this seems the most likely cause. He described a 27-year-old man who had been treated with propylthiouracil for a period of only 10 days when hematuria, hematemesis, and purpura occurred. Findings of all studies were normal except for a blood coagulation time of 42 minutes and a Quick prothrombin concentration of less than 10%. This was corrected and the bleeding controlled with infusion of whole blood and administration of 370 mg. of menadione (vitamin K, Hykinone) sodium bisulfite over a 72-hour period. Goldstein did not attribute these findings to propylthiouracil, but stated that no other apparent cause could be found.

An additional case has recently come to our attention [6] of a 13-year-old girl who developed melena, nosebleeds, hematuria, and purpura after nine weeks of propylthiouracil therapy. Prothrombin time was reported to be 41 minutes. Phytonadione was administered intravenously. We had the opportunity to examine a sample of the plasma from this patient which had been obtained two days after initiation of phytonadione therapy. The combined prothrombin-proconvertin concentration was less than 10% and that of prothrombin alone was about 8%. Eight days later, another sample of this patient's plasma was examined in our laboratory. The Quick prothrombin time was now 16.2 seconds, and addition of normal serum shortened this to 12.7 seconds. Normal, adsorbed plasma had no effect. Combined prothrombin-proconvertin concentration was 75%, and prothrombin concentration was normal. Five days later, and on the subsequent, consecutive four days, the Quick prothrombin time was normal.

Studies done on the patient we are reporting revealed that, of the known factors measured with the prothrombin method of Quick (i. e., prothrombin, proaccelerin, proconvertin, Stuart factor, and fibrinogen), the deficiency was probably limited to prothrombin and proconvertin. In mixing experiments, only plasma or serum containing one or both of these corrected the prolonged prothrombin time of the patient's plasma, and no correction was observed when proconvertin was lacking. This finding lends significant support to a hypothesis of deficiency of proconvertin. That prothrombin also was lacking was shown by the method specific for prothrombin. Experiments such as these were not reported in the cases of Craddock [2a] and Miner,[2b] and, although their conclusions with regard to these deficiencies differ from ours, it seems probable in view of current concepts that these deficiencies were similar to that seen in our patient.

The characteristic response of the coagulation system to administration of bishydroxycoumarin (Dicumarol) is a specific reduction in concentration of prothrombin and proconvertin [7] (plasma thromboplastin component and the thromboplastin-forming stage of coagulation will not be considered here). Similarly, a combination of hypoprothrombinemia and hypoproconvertinemia may occur in severe liver disease.[7] No history of ingestion of bishydroxycoumarin could be elicited from our patient. Liver function tests did not indicate severe liver disease. Evidence of a severe coagulation deficiency together with little or no effect on other systems makes it apparent that the toxic effect of propylthiouracil was directed primarily against the clotting mechanism. The failure of a single administration of phytonadione to induce a permanent correction of the prothrombin time is of interest and may indicate the severity of the deficiency produced.

It is suggested that propylthiouracil may, although infrequently, result in a specific impairment of the coagulation system with a deficiency of prothrombin and proconvertin and that this defect can be corrected by vigorous treatment with parenteral administration of phytonadione.

Summary

A hemorrhagic tendency is a rare but serious manifestation of propylthiouracil toxicity. Our studies suggest that this bleeding tendency arises from a specific dual deficiency of prothrombin and proconvertin. Administration of phytonadione (vitamin K_1 oxide, Mephyton) corrected this deficiency, but repeated administration of this drug was necessary to maintain a normal Quick prothrombin time.

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The blood plasma deficient in proconvertin was supplied by Prof. P. A. Owren, Department of Medicine, Rikshospitalet, Oslo. The blood plasma deficient in Stuart factor was supplied by a patient reported by Gonyea and Krivit.[5]

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ACUTE BLOOD LOSS REQUIRING NINETY-FIVE TRANSFUSIONS

REPORT OF A CASE

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and
John H. Hobika, M.D., Boston

A case of a patient with an endometrial sarcoma that was treated by radical pelvic surgery is of interest because of the manner in which acute loss of blood was managed.

A 43-year-old woman, gravida 3, para 3, was admitted to the New England Center Hospital because of pain and swelling in her lower extremities. For the past three years she had noted irregular, and occasionally profuse, vaginal bleeding. Three weeks prior to admission her right leg became swollen and, more recently, her left. She denied any gastrointestinal or genitourinary symptoms.

Her history revealed that a dilation and curettage had been performed seven years prior to this admission. The pathological diagnosis at that time had been benign secretory endometrium and chronic cervicitis.

Physical examination revealed a blood pressure of 130/80 mm. Hg and a pulse rate of 84 per minute. The chest was clear to percussion and auscultation. The heart sounds were normal, and there were no murmurs. Positive findings were limited to the abdomen, pelvis, and extremities. A firm, tender mass was palpable to the umbilicus. The mass descended into the pelvis where it was fixed, displaced the cervix to the left, and extended to, but did not involve, the pelvic walls. There was no swelling of the extremities.

Laboratory examinations revealed a hemoglobin level of 8.5 Gm. per 100 cc. and a hematocrit of 29.5%. The blood sedimentation rate was 76 mm. per hour (Westergren method). The platelet count was 475,580 per cubic millimeter, and the prothrombin time 100%. The bleeding time was normal. The level of blood urea nitrogen was 12 mg.% and

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that of creatinine 0.5 mg.%. The remainder of the laboratory results, including those of liver function tests and determination of serum electrolytes, were normal.

An intravenous pyelogram revealed what appeared to be an obstruction of the right ureter. There was normal function in the left kidney. The remainder of the roentgenographic studies showed pressure defects secondary to the tumor but no involvement of the gastrointestinal or urinary systems. Findings of an electrocardiogram were normal.

The patient was given a preoperative transfusion of 2,000 cc. of whole blood and the hematocrit, determined immediately preceding operation, was 39.5%. At operation, one week after admission, after a dilation and curettage, a large tumor mass was found, which arose from the fundus of the uterus and invaded the base of the bladder and extended to the pelvic walls. The pelvic veins were filled with "fleshy" material initially thought to consist of thrombi. The hypogastric arteries were ligated and divided, and an anterior exenteration was performed. On the left side a cutaneous ureterostomy was done and the right ureter was ligated. There was persistent bleeding, most of which occurred along the pelvic walls near the greater sciatic notches. Individual vessels were ligated and then oversewn en bloc. Hot packs, pressure packs, and bone wax were applied to the bleeding areas without effect. The hematology service was consulted, and blood was drawn for an evaluation of the clotting mechanism. There was no evidence of a clotting defect or fibrinolysis. The blood loss had reached a critical level in spite of aortic compression and the occlusion of the common iliac vessels with bulldog clamps. Fresh blood, in plastic containers, was given intravenously under pressure into both arms and one leg. The pelvis was finally packed with 27 ft. of 3-in. gauze, one end of which was brought out through the vagina. The wound was closed with through-and-through steel wires in addition to a running suture in the peritoneum and a fine silk suture in the skin. The operative procedure lasted 11 hours. In spite of the normal findings of blood analysis, 9 Gm. of fibrinogen, 40 mg. of conjugated estrogenic substances (Premarin), 200 mg. of cortisone acetate, 7 Gm. of calcium gluconate, and 250 mg. of phytonadione (Mephyton) were given intravenously during the procedure; 92 pints of whole blood was given in the operating room.

At the conclusion of the operation, clear urine was coming from the cutaneous ureterostomy. The patient's blood pressure was 80/60 mm. Hg, and the pulse was weak, with a rate of 72 per minute. The weighed blood loss was 45,000 cc. and its replacement 45,740 cc. When the patient was transferred to the recovery area, blood was oozing from the incision. At 9:30 p.m., two hours after the operation, the blood pressure was 80/45 mm. Hg, and the pulse rate 100 per minute. At 11 p.m., the pulse rate was 80, and the skin was cold; an infusion of 500 cc. of whole blood was started. At midnight the 94th pint of blood was given, and at 4 a.m., the 95th. The blood pressure remained at 80/60 mm. Hg, and the pulse rate was 110 per minute. By 8 a.m. the following morning the bleeding had stopped and the record of vital signs was as follows: blood pressure 124/80 mm. Hg, pulse rate 84 per minute, and respirations 20 per minute; the axillary temperature was 97.8 F (36.6 C). The skin was warm, and the pulse was strong. The patient was alert and cooperative. There was about 15 cc. of urine in the disposable bag attached to the ureterostomy.

Metabolic and hematological consultations were obtained. Examination of the urinary sediment was not suggestive of tubular necrosis, but because of this possibility only small amounts of hypertonic dextrose were given. Levels of serum electrolytes, 12 hours after operation, were as follows: sodium 144 mEq. per liter, potassium 4 mEq. per liter, chloride 83 mEq. per liter, and carbon dioxide 41 mEq. per liter. The hematocrit was 35.5%, and blood urea nitrogen level was 20 mg.%. The rise in carbon dioxide level was thought to be due to the 7,125 cc. of citrate given during the operation. Hematological studies did not reveal clotting defects or abnormal blood indexes. During the first 24 hours after operation, 375 cc. of urine was passed.

By the third postoperative day bowel sounds were present. The electrolyte values improved, and the blood urea nitrogen level reached a high of 26 mg.% on the second postoperative day. The creatinine level, which had been reported as 0.5 mg.% preoperatively, rose to 1.0 mg.% on the second postoperative day and fell to 0.8 mg.% on the fourth postoperative day. The hematocrit fell to a low of 30% on the sixth postoperative day. On the fourth postoperative day 6 ft. of the vaginal pack was removed. The patient complained of pain in the sciatic area as the pack was pulled, and drop foot was noted at this time. No cardiorespiratory complications developed. The lungs remained clear. The electrocardiogram suggested electrolyte disturbance. All of the original pack was removed by the seventh postoperative day. On this day one additional unit of whole blood was given. Normal intestinal activity was present on the eighth postoperative day, and by the ninth day the wound was well healed, and the patient was taking nourishment by mouth. The drop foot improved.

On the 13th day, after removal of the wire stay-sutures, fluid was coming from the vagina. Methylene blue studies revealed leakage of urine from the previously ligated right ureter. An intravenous pyelogram showed marked hydronephrosis on the right, with minimal dilatation of the drainage system on the left side. It was felt that removal of the pack had weakened the ligatures. The ureter was religated by means of a retroperitoneal exposure. The patient tolerated this additional procedure well.

One week later she developed diarrhea. A pelvic abscess was drained per vaginam. One month after operation the pelvic cavity was examined through the vagina with a proctoscope, and a biopsy specimen was taken of the granulating base. The pathological report revealed no evidence of malignancy. One week after the latter procedure the patient developed a temperature of 101 F (38.33 C), and a friction rub was heard in the left posterior lung field. An x-ray of the chest revealed a small amount of fluid at both bases. No chemotherapy was given. The fluid disappeared within four days, and the atient became afebrile. She was discharged afebrile and essentially well, except for residual drop foot on her 41st postoperative day.

The laboratory studies at the time of discharge revealed the following findings. X-ray of the chest and electrocardiogram were normal. The blood urea nitrogen level was 11 mg.% and those of serum electrolytes normal. The hematocrit was 38.5%. Urine culture grew *Proteus vulgaris*, with a colony count of over 10 million organisms per milliliter. Arrangements were made to have the Visiting Nurse Association supervise the care of the ureterostomy and the irrigation of the perineum.

The patient's progress was followed and, at the last office visit, in April, 1959, she had gained 25 lb. (11.4 kg.). The ureterostomy was functioning well, and the drop foot showed continued improvement. A follow-up intravenous pyelogram revealed no function on the right and slight dilatation of the pelvis and ureter on the left side. There had been no significant change since the postoperative pyelogram. A repeat urine culture revealed Proteus vulgaris, 47,000 organisms per milliliter. The hematocrit and the blood urea nitrogen level remained normal.

The final pathological report was as follows: endometrial stromal cell sarcoma, with conspicuous endolymphatic and intravenous extension. Examination of the gross specimen revealed a tumor filling the pelvic veins.

Gardner and associates[1] reported 58 transfusions in connection with a case of placenta percreta in which the control of bleeding was finally accomplished with the application of pneumatic pressure to the lower half of the body. Artz and associates[2] reported on a battle casualty of the Korean war to whom 23,350 cc. of whole blood was given within 24 hours.

The case reported here demonstrates that massive blood transfusion is compatible with life and that renal function, even with one kidney, may survive such an insult. The patient's blood was type A, Rh-positive, and she received only this type during and after operation. The occurrence of drop foot was probably the result of pressure on the sciatic nerve. To our knowledge the amount of blood administered to this patient within a 24-hour period is the largest recorded to the time of writing.

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MANAGEMENT OF THE DEPRESSED PATIENT.—Physicians in all medical specialties are called upon at times to diagnose and to treat patients who are depressed, and who threaten or attempt suicide. Without doubt, many of the acknowledged 16,200 suicides each year in this country are the result of a diagnostic or therapeutic failure with patients suffering from serious depressive illness. (The reported total of 16,200 is very likely only a fraction of the total number: the social stigma of suicide, along with insurance considerations, may result in a great deal of covering up by the patient, his family and others.) The family physician is frequently the person to whom the depressed patient turns prior to making serious self-destructive attempts. . . . In no case should the patient leave the physician's office without being given a definite return appointment. Because of the sleeplessness and agitation usual in this condition, there is a timeless quality present, and the patient should not be left for a long period to his own devices. The physician should not prescribe large doses of medicine of any sort, especially sedatives. Large amounts of barbiturates or tranquilizers make potent weapons. Also, having the patient return at least once every week for refills of medicine represents a fine way to guarantee sustained medical observation.—M. H. Miller, M.D., C. H. Fellner, M.D., and N. S. Greenfield, Ph.D., Depression, Suicide and Suicidal Gesture in Medical Practice, *Annals of Internal Medicine*, July, 1959.

SPECIAL ARTICLE

DEVELOPMENT OF SURGERY IN THE SOUTH

Alton Ochsner, M.D., New Orleans

The South has probably contributed as much to the development of surgery as any other section of the nation. Before the introduction of antisepsis and asepsis and the availability of anesthetic agents, performance of surgical procedures was attended with considerable risk and tremendous suffering. Although the South cannot claim credit for the development of asepsis, ether anesthetization, use of which makes an operation painless, was first used in the South and marks one of the really great milestones in the progress of surgery. Although ether had been synthesized in 1540 and its effects were known to be similar to those of nitrous oxide, it was not until March 30, 1842, that ether was first used for surgical anesthesia when Crawford W. Long at Jefferson, Ga., in Jackson County, removed a tumor from the neck of James W. Venable. However, P. A. Wilhite, of Anderson, S. C., was the first to produce anesthesia with ether, albeit accidentally, in 1841. "The negro boy to whom Dr. Wilhite administered the ether became so profoundly insensible that the Doctor, thinking that he would not recover from the anesthetic, had his horse saddled and intended to escape into Tennessee." [1] Even though Long did not publish the results of his original work until December, 1849, he used ether successfully in eight operations before Morton's contribution in 1846.[2]

Contributions in Gynecology

Surgery was given a tremendous impetus when Ephraim McDowell performed the first successful ovariotomy, on Mrs. Jane Crawford, Dec. 13, 1809. Unfortunately, the report of this was not published until 1817. McDowell reported 13 operations on diseased ovaries with four deaths, eight recoveries, and one failure to complete the operation because of adhesions.[3]

A southerner, Dr. Jessie Bennett, performed the first cesarean section in the United States in Rockham County, Va., on Jan. 14, 1794.[4] The patient was his wife and he used Roussel's textbook as a guide. Both mother and baby recovered. J. L. Redmond of Newtown, Ohio, performed the second cesarean section in the United States in 1827, and the third was performed in Louisiana three years later by Prevost, who performed three others, with the loss of only one mother; he performed cesarean section on one woman twice.[5] In 1816, John King, of South Carolina, operated on a woman with extrauterine pregnancy by incising the vaginal wall and applying pressure on the abdomen above and forceps to the fetus; both mother and child survived.[6] In 1813, Joseph Glover of South Carolina successfully performed a hysterectomy.[1] Also on Aug. 12, 1801, he performed the first splenectomy, with recovery of the patient.[1]

Another gynecologic operation developed by a southerner, J. Marion Sims, a native South Carolinian, practicing in Montgomery, Ala., was correction of vesicovaginal fistula. In 1845 he first advocated the knee-elbow (Sims) position and fashioned a duck-bill speculum from a pewter spoon which enabled visualization of the fistulous opening.[2] After experimenting with many techniques of closure of vesicovaginal fistulas, he concluded that previous failures had been due to use of silk sutures that had become infected, so he used pure silver sutures with success. Although Sims is best known for his gynecologic contributions, he successfully operated on a patient with a hepatic abscess in 1835, successfully removed the mandible from a mouth in 1837, and removed the maxilla because of carcinoma of the antrum. In 1878, he probably did the first cholecystotomy for biliary calculi in the South. This was 10 years after the operation had been originally performed by J. S. Bobbs, of Pennsylvania, although Sims was unaware of Bobbs' operation.

In 1900 Cartledge, of Louisville, discussed mammoth ovarian tumors and described a cyst weighing 245 lb. He was a prolific writer and did considerable investigation on surgery of the gallbladder and intestinal tract.[7]

Pioneers in Urology

One of the early operations performed in the South was lithotomy. Benjamin W. Dudley, a native of Virginia, who had considerable training in Europe, returned to Lexington, where he became professor of anatomy and surgery at Transylvania University in 1819. He was one of the best-known lithotomists of his time. He performed more than 225 lithotomies and had a consecutive successful series of 100. In addition he treated, by trephina-

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Read before the Section on Surgery, General and Abdominal, at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

tion, six patients with posttraumatic epilepsy, four of whom were cured.[3] His first patient was treated in 1819, which, according to Gross,[8] was the first in America. In 1852 Hardin, of Louisville, also reported relief of symptoms after trephination in patients with posttraumatic epilepsy.[8] Dudley was the first surgeon to treat fungus cerebri by sustained and gentle pressure with a dry sponge maintained in place by roller bandage.[3] He popularized use of roller bandages in the treatment of many surgical conditions, such as edema associated with infection and trauma.

Other contributions to urology were by Gilmore,[9] of Mobile, Ala., who, in 1871, reported a case of successful nephrectomy performed on a woman in December, 1870, and by J. Marion Sims,[2] who devised a special catheter for emptying the bladder which could be used during healing after repair of vesicovaginal fistula.

Southerners Perform First Amputations in the United States

In 1806 Walter Brashear,[9] of Lexington, was the first person in America to perform amputation at the hip. Although this operation had been unsuccessfully performed by Kerr in England in 1744, Brashear had no knowledge of it. He had considerable experience in the treatment of diseases of the bones and joints and in trephining for fractures of the skull. He subsequently moved to Louisiana and became a United States senator. In 1810 Deaderick,[10] of Tennessee, performed a hemimandibulectomy, presumably for cystic disease of the mandible.

Apparently amputations were rather common operations early in United States history. Eve,[11] writing in 1846, was distressed by the fact that Europeans considered that the mortality after performance of amputation in the United States was extremely high. He reported successful results in performing seven amputations of the leg and seven of the thigh. He emphasized the importance of compression bandages in order to prevent "both hemorrhage and inflammation."

In 1852 Gross,[12] professor of surgery at the University of Louisville, reported complete or partial resections of the mandible in seven patients and of the inferior maxilla in five patients. All of the former did well and four of the latter died. In 1850 Gross [13] resected most of the scapula, for an osteosarcoma. Robert A. Kinloch, professor of surgery at the South Carolina Medical College, was the first person in America to wire a fracture of the mandible successfully and to resect a knee joint.[14] In 1857 Parker [1] reported excision of the hip joint for tuberculosis. In 1811 McCreary, of Kentucky, resected the clavicle for osteosarcoma.[8] Nott [15] of Mobile, Ala., first described coccygodynia and successfully treated the condition by extirpation of the coccyx in May, 1844.

Tobias G. Richardson, professor of surgery at Tulane University, performed the first successful amputation of both legs at the hip joint in one stage.[5] Schupert, also of New Orleans, early removed the scapula for malignant disease.[8] In 1825 Robert B. Butt, of Virginia, resected the lower two-thirds of the ulna. Chopin, of New Orleans, removed the entire radius and, in 1853, Compton, also of New Orleans, removed the radius and all but the inferior extremity of the ulna.[8] Carnochan, of Savannah, resected the ulna in 1853,[16] the radius in 1854 [17] and the os calcis in 1857.[18] In 1913, Parham and Martin, of New Orleans,[19] described a metallic band for use in oblique fractures.

Important Contributions in Orthopedic Surgery

Of importance in the diagnosis of dislocation of the shoulder was an observation made by Dugas [20] in 1856. He considered the following criterion unequivocal evidence of dislocation of the shoulder: "If the fingers of the injured limb can be placed [by the patient or the surgeon] upon the sound shoulder while the elbow touches the thorax there can be no dislocation and if this cannot be done, there must be a dislocation."

Barney Brooks of Washington University, subsequently chairman of the department of surgery at Vanderbilt University, did considerable work on bone regeneration and bone growth. In 1924 he [21] performed the first arteriography in the United States. In addition to considerable work on Volkmann's ischemia and intestinal obstruction, he [22] was without doubt one of the best teachers of surgery. Venable and associates [23] of San Antonio, Texas, experimentally showed the effects of electrolysis of bone produced by certain metals and introduced Vitallium as a safe metal.

Early Success in Removal of Tumors

Eve,[24] of Georgia, reported local removal of a giant polypus from the base of the cranium in 1836. Its recurrence necessitated resection of the maxilla and palatine plate of the palate. George Cupples, of Texas, was the first in the United States to extirpate the tongue for cancer, according to Nunnally's method.[25] Cupples was also chairman of a committee on surgery of the Texas State Medical Association, which in 1872 reported a mortality of 8% among 4,293 operations performed in Texas.[26] Gilmore,[9] of Mobile, reported four cases of excision of the tongue for carcinoma.

In the early part of the last century, Charles A. Luzenberg, one of the founders of the University of Louisiana (which is a forerunner of Tulane University), its first dean and professor of surgery, removed a tumor of the parotid [27]; L. M. Tiffany, of Maryland, in 1878 successfully removed a large nasopharyngeal polyp,[28] and in 1886 he [29] removed a tumor of the liver. Parker,[1] of Charleston, S. C., was the first surgeon in the United States to suture a divided nerve successfully, and he reported this in 1881.

Surgery of the Chest and Abdomen

Although relatively rare, thoracic operations were performed before the introduction of anesthesia and asepsis. Early in the last century Warren Stone, of New Orleans, was one of the first persons deliberately to resect a rib for drainage in empyema.[5] Antony,[30] of Georgia, in 1821, operated on a boy for necrosis of the rib and empyema, which were complications of an injury sustained three years previously. The overlying ribs and most of the lung were excised. It was necessary to remove additional portions later. Not less than two-thirds of the right lung had been removed. The patient did well after the removal of all the ribs from the fifth to the diaphragm, but measles subsequently developed and the patient died on July 11, 1822.

As in surgery of the thoracic cavity, surgery of the abdomen was rarely attempted before the introduction of anesthesia and asepsis. Gross, in 1843, and Sims, just shortly before his death, suggested laparotomy in the treatment of penetrating gunshot and stab wounds, but neither was able to use it.[1] However, in July, 1867, Kinloch,[31] of Charleston, reported a case of a Confederate soldier in whom he successfully resected the injured intestine and reestablished intestinal continuity. In 1835 Luzenberg, of New Orleans, performed the first successful resection of a gangrenous intestine associated with strangulated hernia, with reestablishment of intestinal continuity.[5]

Halsted, as professor of surgery at Johns Hopkins University, probably exerted a greater influence on surgical training than anyone else in the world. He introduced the experimental method of teaching surgery as well as the present concept of residency training. His fundamental work on intestinal and vascular anastomoses, conduction anesthesia, and development of original operations for the cure of inguinal hernia, cancer of the breast, and thyroid disease make him almost an immortal surgeon. He also introduced use of rubber gloves in the operating room because his surgical nurse, who subsequently became Mrs. Halsted, was allergic to the frequently used bichloride of mercury. In 1898 he performed the first successful operation for carcinoma of the ampulla of Vater.[2] In 1906 he demonstrated that tetany could be treated successfully by transplantation of parathyroid tissue.[32]

Another colorful figure at Johns Hopkins was Joseph C. Bloodgood, a native of Wisconsin, who spent his entire professional career at the Johns Hopkins Hospital. He probably did more than anyone else to put surgical pathology on a scientific basis, and he exerted tremendous effort in the development of oncology.

Herff,[33] of San Antonio, a native of Germany, performed the first gastrostomy in America on Aug. 31, 1879, using the technique of Howse. Thompson,[34] a native of England, as the first professor of surgery at the University of Texas, did much to advance the practice of surgery. His publications on the surgical approach to the bones of the extremities, embryology, tumors of the neck and general surgical subjects are classics. His successor, Albert O. Singleton, did a great deal of work on abdominal incisions, wound disruptions, and surgery of the intestinal and lymphatic systems.[35]

More recently, intra-abdominal surgery has been greatly advanced by John M. T. Finney,[36] of Johns Hopkins, who did much to establish, on a rational basis, the surgical treatment of gastrointestinal disease. He described the pyloroplasty which bears his name. Le Grande Guerry,[37] of Columbia, S. C., emphasized early, by his own results, the feasibility of decreasing the mortality in appendicitis and penetrating wounds of the abdomen. He was the first to use ordinary cotton in subcutaneous areas. Irvin Abell of Louisville, Ky., did much to standardize gastrointestinal surgery, as did W. D. Haggard [38] of Vanderbilt University. J. Shelton Horsley,[39] a prolific writer, did much original investigative work on surgery of the gastrointestinal tract and vascular system. Frederick W. Rankin,[40] a native of North Carolina, did more than anyone else in the United States to standardize the rational treatment of diseases of the colon, and his original investigations on thyroid disease are fundamental. His contributions to the World War II effort were tremendous. Harvey Stone [41] of Johns Hopkins University made notable contributions to intestinal surgery and did fundamental work on transplantation of the thyroid and parathyroid glands.

Development of Vascular Surgery

Vascular surgery has developed tremendously in the South, possibly due to the fact that vascular injuries probably occur more often in the southern areas than in other portions of the United States. Unquestionably, the large number of patients with stab wounds admitted to the charity hospitals in New Orleans, Atlanta, and Houston offer considerable opportunity for the treatment of vascular injuries. One of the great difficulties in operating on vascular injuries and other lesions, such as aneurysms, before the introduction of asepsis, was the danger of subsequent hemorrhage. It was the custom to leave the wounds open and allow the ends of the ligatures to extend out of the wound so that they could be removed. In order to determine whether metal sutures might be used, in 1828, Levert,[42] of Mobile, Ala., did extensive investigation on animals. Acting on the suggestion of Dr. Physick that lead ligatures might be well tolerated because bullets remain in contact with

COMMITTEE ON COSMETICS

Report to the Committee

The management of facial disfigurements has become a more acute medical problem, with greater recognition of the social and economic handicaps consequent to physical deviations from what is considered normal. It is becoming increasingly apparent that the presence of facial disfigurements, which cannot be successfully masked through cosmetic measures, more often than not may mean marginal or minority status in our society.

These pressures, added to the mass media publicity of improvements in dermatological and surgical techniques, have created a greater public demand for facial rehabilitation.

It is for this reason that the Committee sponsored the symposium, "The Management of Cutaneous Facial Disfigurements" at the 108th Annual Meeting of the American Medical Association in Atlantic City, June 9, 1959. This is the first in a series of papers that will appear in The Journal. Veronica Lucey Conley, Ph.D., *Secretary.*

DERMABRASION FOR THE IMPROVEMENT OF ACNE SCARS

Herbert Rattner, M.D.
and
Paul Lazar, M.D., Chicago

[illegible] discussing the value of dermabrasion for the [illegible]ment of acne scars, there is a temptation, [illegible]ally, either to endorse it or to condemn it [illegible] qualification. In the six years since Kurtin[1] reported on the method, it has been used on [illegible] thousand patients by a large number of [illegible]. Modifications and improvements have [illegible] introduced and experiences and results re[illegible]. Still the merits of dermabrasion as a pro[illegible] are viewed with varying degrees of pessi[illegible] or enthusiasm. We believe that the method [illegible] considerable merit and unfortunate limi[illegible] and we undertake herein to assess it on the [illegible] our experience in as realistic a manner as [illegible]

[illegible] are the merits? It is an office procedure. [illegible] is no need for hospitalization. There is no [illegible] general anesthetic. The technique is sim[illegible] relatively free from hazards; there is no [illegible] the morbidity is tolerable, and, in well [illegible], the results are quite satisfactory and [illegible] source of a great deal of happiness to [illegible]

[illegible] of scars can be improved (fig. 1), and [illegible] type for treatment is encountered [illegible]. Too often the results fall short [illegible] expectations, and, in such cases, if [illegible] the basis for unhappiness, this [illegible] ungrounded.

[illegible] procedure was piqued some [illegible] of this rather the late Dr. Abner Kurtin. At the time, one of us (H. R.) communicated with several dermatologist-colleagues in New York whose replies were critical of the method on two grounds: the results that they had observed were disappointing, and the use of ethyl chloride, the refrigerant in use at the time, was hazardous. Besides these objections, there was the generally held view that, though unfortunate, acne scars were of not too great importance and did not warrant such drastic treatment. We did not pursue the subject, and our interest waned, though patients continued to inquire about the method. Two years later, during a meeting of the American Academy of Dermatology in Chicago, we discussed the matter with the late Dr. Rein of New York, who, like Kurtin, had been using the procedure and had found it worthwhile in many instances. He suggested a visit to New York, for he stated that the "results must be seen, they cannot be described." He generously arranged for an opportunity to watch the treatment of a few patients and to examine a number of persons who had previously been treated, in order to compare their skins with their preoperative photographs. The first impressions were mixed. The results, it appeared, hardly warranted the considerable amount of trouble involved, and yet, curiously, the patients all expressed satisfaction. This was difficult to comprehend then, just as it is today by physicians who have not themselves used this method. Later, two young women were presented, with practically flawless skin. In fact, it was a genuine surprise to be told that their skins had been planed some months previously. Their [illegible]rative photographs showed their scars to

Tulane University, and Dan Elkin, of Emory University, in Atlanta. Both Dr. Gage and Dr. Elkin helped standardize the treatment of traumatic and arterial aneurysms and arteriovenous fistulas. Dr. Gage also did considerable work on the systemic effects of arteriovenous anastomoses.

Still more recent research in vascular surgery has been conducted by Alfred Blalock, who began his investigations while at Vanderbilt University but who consummated these after assuming the professorship of surgery at Johns Hopkins University. In 1944 Blalock performed his first shunt operation for tetralogy of Fallot.[41] Smithy, of South Carolina, did much to rationalize the therapy of constrictive valvular disease. As early as 1950 he and his associates[50] reported eight mitral valvulotomies with only two deaths, a remarkable feat at that time.

Michael DeBakey, originally working in the experimental laboratories at Tulane University and the wards at Charity Hospital in New Orleans, did considerable fundamental work on arterial and venous diseases, and after assuming the chairmanship of the department of surgery at Baylor University, he made practical restoration of vascular continuity in patients suffering from aneurysmal and obliterative disease of the aorta and other vessels. He and his associates, more than anyone else, have standardized the technique of replacement of diseased vessels with either homogenous or synthetic grafts.

Southern Contributions to Medical Education

The South also has contributed its share to the teaching of medicine and to organized medicine. Eve, of Georgia, might well be called a peripatetic professor.[6] In 1832 he was professor of surgery at the Medical College of Georgia. Later he became professor of surgery at the University of Louisville, still later at the University of Nashville, and, finally, at the Missouri Medical College in St. Louis.

Yandell, a native of Tennessee, who returned to Louisville in 1869 to become professor of surgery at Louisville after two years' training in Europe, did much to foster publications of medical literature.[51] He started the *American Practitioner* in 1870, which he edited until 1886, when it merged with the *Medical News* to become the *American Practitioner and News.* This he edited until his death in 1898. He was president of both the American Medical Association and the American Surgical Association.

Although he is usually not considered a southerner, Gross[52] spent much of his active teaching period in the South as professor of surgery at the University of Louisville, which post he assumed in 1840, when it was the Louisville Medical Institute. He remained there for 16 years except for one year when he was professor of surgery at the University of the City of New York. He stayed at Louisville until 1856, when he accepted the position of professor of surgery at Jefferson Medical College. While in Louisville he did considerable work on diseases of the urinary tract. He wrote "A Treatise on Disease of the Urinary Bladder, the Prostate Gland and Urethra" and also "A Practical Treatise on Foreign Bodies of the Air Passage." This was the most classic article written at that time. Although the work was completed in 1859, after he returned to Jefferson Medical College, he did much of the writing on his system of surgery in Louisville. Gross was President of the American Medical Association in 1868 and was one of the founders of the American Surgical Association, of which he also became president.

McGuire of Richmond, Va., one of the founders of the Medical College of Virginia at Richmond, was extremely interested in medical education.[52] He did considerable investigation on prostatic hypertrophy. He was one of the founders of the American Surgical Association and was President of the American Medical Association in 1893.

John M. T. Finney, who was active during World War I, carried a tremendous teaching load at Johns Hopkins. He was the first president of the American College of Surgeons, one of the founders of the Society of Clinical Surgery, and president of the Southern Surgical Association in 1912 and of the American Surgical Association in 1921.

Fred Rankin was President of the American Medical Association, the American Surgical Association, and the American College of Surgeons. William D. Haggard, who made a great contribution to the war effort in World War I, was President of the American Medical Association, the American College of Surgeons, and the Southern Surgical Association.

Irvin Abell of Louisville, who did much to standardize surgery, was President of the American Medical Association, the Southern Surgical Association, and the American College of Surgeons. Dr. Matas was one of the 12 founders of the American College of Surgeons, and its president in 1925 and 1926; he received an honorary fellowship from the College in 1952. He was president of the American Surgical Association in 1900, the Southern Surgical and Gynecological Association in 1910, the American Association of Thoracic Surgery in 1920, and the International Society of Surgery in 1936. He received the first certificate of merit awarded by the American Medical Association.

From this kaleidoscopic review it is evident that the South, although more isolated than the eastern portion of the United States, has made a notable contribution to the progress of American surgery. This is a heritage in which we can have justifiable pride.

3503 Prytania St. (15).

tissue for long periods of time without producing irritation, he decided to use such material. In all, he experimented with lead, gold, platinum, and rubber ligatures. He came to the conclusion that metal ligatures are well tolerated. In 1841 Dudley successfully ligated the carotid in a 25-year-old man with pulsating exophthalmos; in 1825 he ligated the subclavian artery for an axillary aneurysm.[13] In 1857 Dugas [43] operated on a boy for traumatic aneurysm of the sciatic artery, but secondary infection and severe hemorrhage developed postoperatively. Because this continued, the common iliac artery was ligated, but unfortunately the patient died. Warren Stone, of New Orleans, was the first to use a metallic ligature in 1859 when he ligated the common iliac artery for an external iliac aneurysm with silver wire. Smyth,[44] also of New Orleans, performed the first successful ligation of the innominate artery. On May 16, 1864, he ligated the innominate artery one inch above the clavicle. However, severe hemorrhage occurred, and the wound was packed with shot; six weeks later the patient almost died of hemorrhage. On July 8 the vertebral artery was ligated. The patient was apparently cured for 10 years, but then the aneurysm recurred. The internal mammary artery was ligated without benefit and an attempt to plug the openings was made, but the patient died of hemorrhage 48 hours later. On June 9, 1866, Mastin,[45] of Mobile, ligated the external iliac, 0.5 in. below the bifurcation, with a no. 32 silver wire, in a patient with an inguinal aneurysm. He repeated Levert's experiments, using metal sutures and confirming Levert's result. Although Rehn, in Frankfurt-am-Main, performed the first successful operation for cardiac injury in the human being in 1896, this operation was first successfully performed in the United States by Hill,[46] of Montgomery, Ala., the father of the illustrious senator from Alabama. At one o'clock in the morning on Sept. 9, 1902, in a rural shanty, he operated on a 13-year-old boy who had a stab wound of the heart.

Whereas the foregoing contributions to vascular surgery are of extreme importance, the greatest contributions in this field were made by Dr. Rudolph Matas of New Orleans.[47] Dr. Matas was justly designated by Dr. William Mayo as the world's best-educated physician. While an intern at the Charity Hospital in New Orleans in 1880, he assisted at the first laparotomy performed under listerian ritual, which included use of carbolic acid spray.

Dr. Matas' first endoaneurysmorrhaphy was performed on May 6, 1888, for a large traumatic aneurysm in the middle third of the brachial artery. An attempt has been made to control the aneurysm by use of compression, but the aneurysm increased in size and operation was decided on. The brachial artery was ligated in the upper third, just below the profunda and immediately above the aneurysm. Pulsation in the aneurysm ceased and the condition improved. Nine days later slight pulsation recurred, and this increased progressively until the tumor became as painful as it had been at first. Two weeks after the proximal ligation the vessel was ligated below the aneurysm with no decrease in pulsation. The aneurysm was then opened, and three openings in the aneurysmal cavity were sutured. The patient recovered completely. In commenting on this case, 10 years later, Dr. Matas made the following statement.

> At the time this operation was performed, I had no precedent to guide me, the only work that had been done, was that of Glueck, published in *Langenbeck's Archives,* in which he detailed 19 experiments in the suture of arteries which had failed to a great extent in spite of ingenious methods that he had devised. The exigencies of the case, however, made it necessary that hemostasis should be obtained, and the occlusion by suture appeared to be so easy and plain that it seemed to me that any surgeon similarly situated would have instinctively adopted the simple way of getting out of the difficulty.

In 1902 Dr. Matas presented four cases of endoaneurysmorrhaphy before the American Surgical Association. He and his associates did considerable experimental work on animals and devised an aluminum band for temporary occlusion of vessels to determine whether collaterals were sufficient. In April, 1923, he performed the first recorded aortic ligation for an aortic aneurysm. The aneurysm became quiescent, although apparently the ligation was not complete. The patient was well for more than a year but died of pulmonary hemorrhage from tuberculous cavitation. Dr. Matas also devised the hyperemic test to determine the adequacy of collateral circulation after obliteration of a vessel.

In addition to his work on the arterial system, Dr. Matas did considerable investigation on the venous system and did more than anyone in the United States to emphasize the role played by edema in the production of recurrent erysipeloid infections of the extremities. His report [48] in 1913 is still a classic and should be read by all students of the subject. He performed the first Kondoleon operation in the western hemisphere, only three months after Kondoleon's original publication in the *Zentralblatt fur Chirurgie* in 1912. Dr. Matas also did considerable work on primary thrombosis of the axillary veins and emphasized the role of effort or strain in its development. He was extremely interested in thromboembolism. He called attention to the tremendous increase in its incidence and considered it a disease associated with modern surgery.

In 1890 Branham,[49] practicing in Brunswick, Ga., described the bradycardiac reflex, which bears his name, after observing it when the blood flow through an arteriovenous aneurysm was interrupted.

Other surgeons in more recent times who have made noteworthy contributions to the treatment of vascular diseases and injuries are Mims Gage, of

Tulane University, and Dan Elkin, of Emory University, in Atlanta. Both Dr. Gage and Dr. Elkin helped standardize the treatment of traumatic and arterial aneurysms and arteriovenous fistulas. Dr. Gage also did considerable work on the systemic effects of arteriovenous anastomoses.

Still more recent research in vascular surgery has been conducted by Alfred Blalock, who began his investigations while at Vanderbilt University but who consummated these after assuming the professorship of surgery at Johns Hopkins University. In 1944 Blalock performed his first shunt operation for tetralogy of Fallot.[41] Smithy, of South Carolina, did much to rationalize the therapy of constrictive valvular disease. As early as 1950 he and his associates[50] reported eight mitral valvulotomies with only two deaths, a remarkable feat at that time.

Michael DeBakey, originally working in the experimental laboratories at Tulane University and the wards at Charity Hospital in New Orleans, did considerable fundamental work on arterial and venous diseases, and after assuming the chairmanship of the department of surgery at Baylor University, he made practical restoration of vascular continuity in patients suffering from aneurysmal and obliterative disease of the aorta and other vessels. He and his associates, more than anyone else, have standardized the technique of replacement of diseased vessels with either homogenous or synthetic grafts.

Southern Contributions to Medical Education

The South also has contributed its share to the teaching of medicine and to organized medicine. Eve, of Georgia, might well be called a peripatetic professor.[6] In 1832 he was professor of surgery at the Medical College of Georgia. Later he became professor of surgery at the University of Louisville, still later at the University of Nashville, and, finally, at the Missouri Medical College in St. Louis.

Yandell, a native of Tennessee, who returned to Louisville in 1869 to become professor of surgery at Louisville after two years' training in Europe, did much to foster publications of medical literature.[51] He started the *American Practitioner* in 1870, which he edited until 1886, when it merged with the *Medical News* to become the *American Practitioner and News*. This he edited until his death in 1898. He was president of both the American Medical Association and the American Surgical Association.

Although he is usually not considered a southerner, Gross[52] spent much of his active teaching period in the South as professor of surgery at the University of Louisville, which post he assumed in 1840, when it was the Louisville Medical Institute. He remained there for 16 years except for one year when he was professor of surgery at the University of the City of New York. He stayed at Louisville until 1856, when he accepted the position of professor of surgery at Jefferson Medical College. While in Louisville he did considerable work on diseases of the urinary tract. He wrote "A Treatise on Disease of the Urinary Bladder, the Prostate Gland and Urethra" and also "A Practical Treatise on Foreign Bodies of the Air Passage." This was the most classic article written at that time. Although the work was completed in 1859, after he returned to Jefferson Medical College, he did much of the writing on his system of surgery in Louisville. Gross was President of the American Medical Association in 1868 and was one of the founders of the American Surgical Association, of which he also became president.

McGuire of Richmond, Va., one of the founders of the Medical College of Virginia at Richmond, was extremely interested in medical education.[52] He did considerable investigation on prostatic hypertrophy. He was one of the founders of the American Surgical Association and was President of the American Medical Association in 1893.

John M. T. Finney, who was active during World War I, carried a tremendous teaching load at Johns Hopkins. He was the first president of the American College of Surgeons, one of the founders of the Society of Clinical Surgery, and president of the Southern Surgical Association in 1912 and of the American Surgical Association in 1921.

Fred Rankin was President of the American Medical Association, the American Surgical Association, and the American College of Surgeons. William D. Haggard, who made a great contribution to the war effort in World War I, was President of the American Medical Association, the American College of Surgeons, and the Southern Surgical Association.

Irvin Abell of Louisville, who did much to standardize surgery, was President of the American Medical Association, the Southern Surgical Association, and the American College of Surgeons. Dr. Matas was one of the 12 founders of the American College of Surgeons, and its president in 1925 and 1926; he received an honorary fellowship from the College in 1952. He was president of the American Surgical Association in 1900, the Southern Surgical and Gynecological Association in 1910, the American Association of Thoracic Surgery in 1920, and the International Society of Surgery in 1936. He received the first certificate of merit awarded by the American Medical Association.

From this kaleidoscopic review it is evident that the South, although more isolated than the eastern portion of the United States, has made a notable contribution to the progress of American surgery. This is a heritage in which we can have justifiable pride.

3503 Prytania St. (15).

COMMITTEE ON COSMETICS

Report to the Committee

The management of facial disfigurements has become a more acute medical problem, with greater recognition of the social and economic handicaps consequent to physical deviations from what is considered normal. It is becoming increasingly apparent that the presence of facial disfigurements, which cannot be successfully masked through cosmetic measures, more often than not may mean marginal or minority status in our society.

These pressures, added to the mass media publicity of improvements in dermatological and surgical techniques, have created a greater public demand for facial rehabilitation.

It is for this reason that the Committee sponsored the symposium, "The Management of Cutaneous Facial Disfigurements" at the 108th Annual Meeting of the American Medical Association in Atlantic City, June 9, 1959. This is the first in a series of papers that will appear in THE JOURNAL.

VERONICA LUCEY CONLEY, PH.D., *Secretary.*

DERMABRASION FOR THE IMPROVEMENT OF ACNE SCARS

Herbert Rattner, M.D.
and
Paul Lazar, M.D., Chicago

In discussing the value of dermabrasion for the improvement of acne scars, there is a temptation, generally, either to endorse it or to condemn it without qualification. In the six years since Kurtin[1] first reported on the method, it has been used on several thousand patients by a large number of physicians. Modifications and improvements have been introduced and experiences and results recorded. Still the merits of dermabrasion as a procedure are viewed with varying degrees of pessimism or enthusiasm. We believe that the method has both considerable merit and unfortunate limitations, and we undertake herein to assess it on the basis of our experience in as realistic a manner as we can.

What are the merits? It is an office procedure, and there is no need for hospitalization. There is no need for a general anesthetic. The technique is simple; it is relatively free from hazards; there is no mortality; the morbidity is tolerable, and, in well selected cases, the results are quite satisfactory and may be the source of a great deal of happiness to the patient.

Not all types of scars can be improved (fig. 1), and the unfavorable type for treatment is encountered all too frequently. Too often the results fall short of the patient's expectations, and, in such cases, if the scars were the basis for unhappiness, this unhappiness is compounded.

Our interest in the procedure was piqued some 10 years ago when we first heard of this rather startling method being used in New York City by the late Dr. Abner Kurtin. At the time, one of us (H. R.) communicated with several dermatologist-colleagues in New York whose replies were critical of the method on two grounds: the results that they had observed were disappointing, and the use of ethyl chloride, the refrigerant in use at the time, was hazardous. Besides these objections, there was the generally held view that, though unfortunate, acne scars were of not too great importance and did not warrant such drastic treatment. We did not pursue the subject, and our interest waned, though patients continued to inquire about the method. Two years later, during a meeting of the American Academy of Dermatology in Chicago, we discussed the matter with the late Dr. Rein of New York, who, like Kurtin, had been using the procedure and had found it worthwhile in many instances. He suggested a visit to New York, for he stated that the "results must be seen, they cannot be described." He generously arranged for an opportunity to watch the treatment of a few patients and to examine a number of persons who had previously been treated, in order to compare their skins with their preoperative photographs. The first impressions were mixed. The results, it appeared, hardly warranted the considerable amount of trouble involved, and yet, curiously, *the patients all expressed satisfaction.* This was difficult to comprehend then, just as it is today by physicians who have not themselves used this method. Later, two young women were presented, with practically *flawless skin.* In fact, it was a genuine surprise to be told that their skins had been planed some months previously. Their preoperative photographs showed their scars to

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Professor of Dermatology (Dr. Rattner) and Assistant Professor in Dermatology (Dr. Lazar), Northwestern University Medical School.

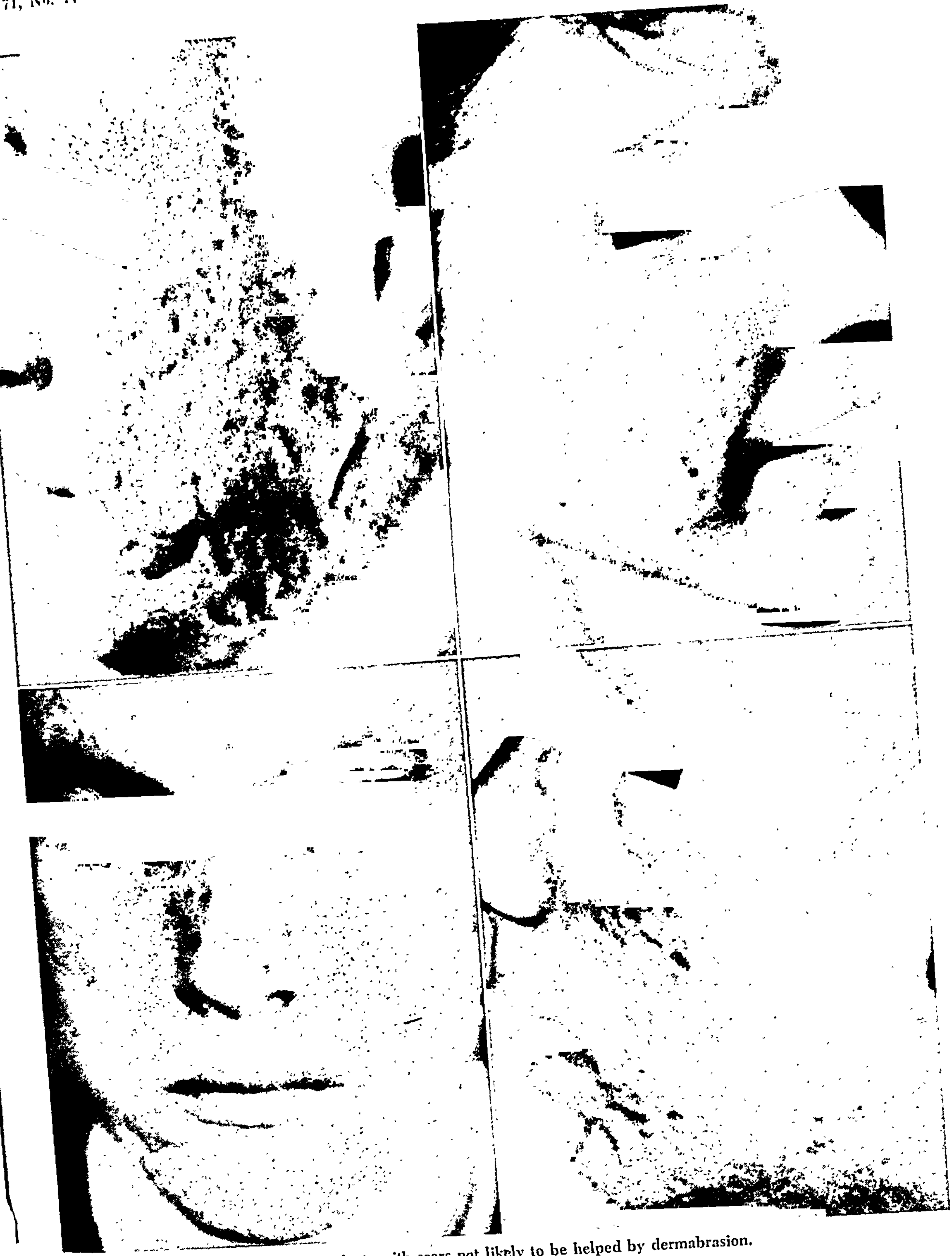

Fig. 1.—Patients with scars not likely to be helped by dermabrasion.

have been flat—like those from chickenpox, but more superficial. This suggested that results from dermabrasion might be dependent upon the shape and depth of the scars treated. An identical experience on the next day in the late Dr. Kurtin's office strengthened that impression. The satisfaction expressed by all the patients and the striking objective improvement in some of them stimulated our interest anew, and we decided to use the method.

It was evident at once that the method was unquestionably the best one yet devised for the treatment of acne scars. In the past, numerous measures had been tried, including scarification, electrodesiccation, surgical excision, surgical shaving, chemical caustics, cryoslush therapy, and the widely publicized abrasion with sandpaper, but all procedures had been found wanting.

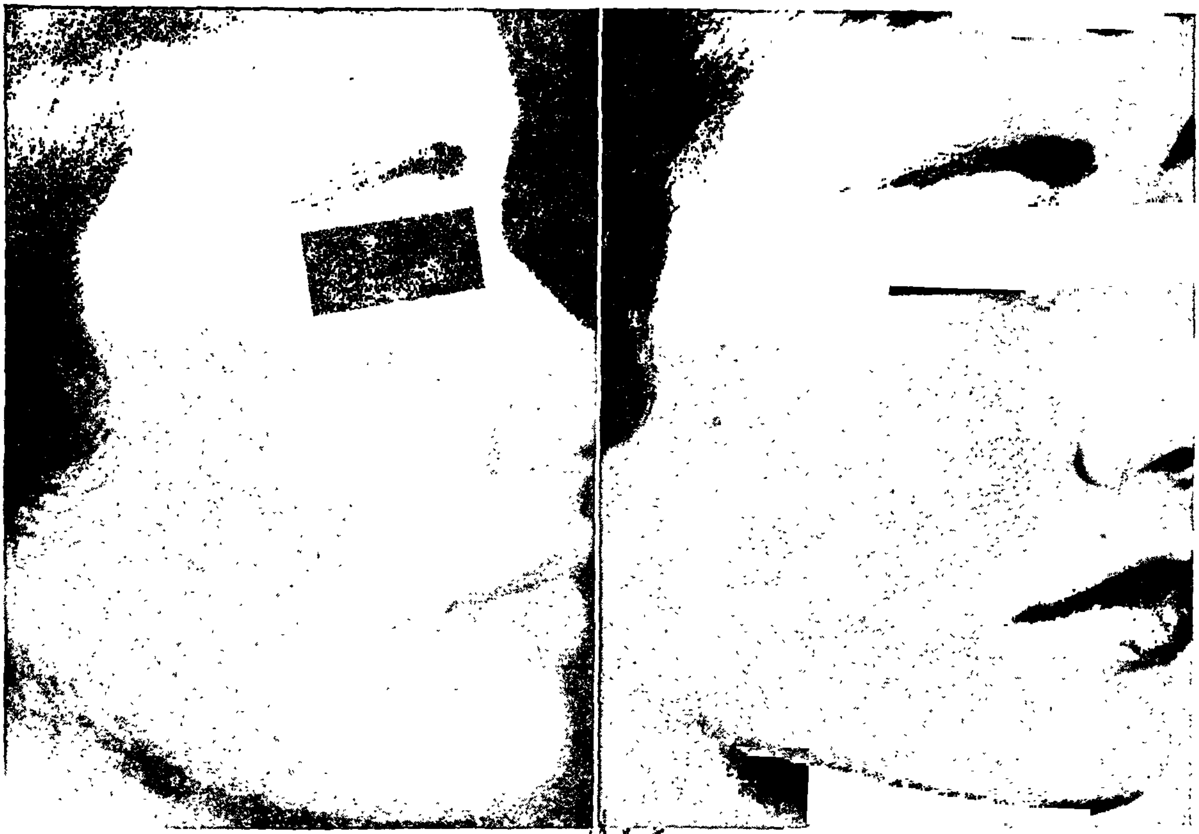

Fig. 2.—*Left*, patient before dermabrasion and, *right*, same patient after dermabrasion.

It was evident, also, that Kurtin's most significant contribution was not the much heralded wire brush, but rather the use of ethyl chloride, for, aside from the anesthesia that was produced, ethyl chloride stiffened the skin to provide an immobile, practically bloodless operative field. This, in our opinion, constituted the real advantage of his method over others previously used. Inevitably, as more physicians gained experience with dermabrasion, innovations and modifications were introduced. In our opinion, the most valuable was the introduction by Wilson, Luikart, and Ayers[2] of dichlorotetrafluoroethane (Freon) to replace ethyl chloride and the suggestion by Hubler[3] to dot the base of each acne pit with gentian violet solution. The dichlorotetrafluoroethane, which is supplied in handy spray-type containers, carries no hazards of explosion or of inhalation, for it has no general anesthetic properties; it does away with the need for a noisy air blower, for plugging the nostrils, and for air passage tubes in the mouth, which always caused discomfort and a great deal of apprehension. Furthermore, it does not cause the dye to run and so mask the operative field. Painting the base of each scar with solution of gentian violet affords an excellent guide and guard against planing too deeply.

Equipment and Technique

The equipment consists of a motor-driven abrading device attached to a stand with a flexible shaft. An adjustable, removable handpiece, similar to a dentist's drill, which will hold an abrading device is attached to the shaft. A foot-operated rheostat controls the rotary speed of the abrading device.

The technique is simplicity itself. A sedative is administered 30 minutes prior to the surgery. Chilled packs, containing a 5% solution of propylene glycol, are applied to clean skin (freshly shaved, cosmetics removed) for about 20 minutes. The scalp is covered with an operating cap or a bathing cap because, should hairs be caught in the rotary abrading device, the handpiece spring may snap. The ear canals are plugged with cotton, the eyelids covered, and the lips greased. The base of each pit is dotted with gentian violet solution to serve as a guide for planing depth. The patient is draped with a clean sheet.

A spray of rapidly volatilizing dichlorotetrafluoroethane is directed to the scarred area, and almost immediately the area becomes frosted, anesthetized, and almost rigid. A wooden tongue blade, held with the operator's free hand, permits him to apply enough tension to make the skin taut. The area is then abraded, by using short, firm strokes in a direction perpendicular to the rotating direction of the brush in order to avoid grooving. The operator then proceeds progressively from area to area until all the scars have been treated and all the gentian violet brushed away. It is better to complete the abrasion of each area with one brushing, for refreezing the skin causes an undesirable postoperative burning sensation and delayed healing. Such matters as the amount of pressure to apply, the width of the abrading brush, the angle at which to hold it, and the direction in which to guide it are all dictated by experience and judgment. As the skin thaws, blood oozes from the treated sites, but it is minimal and ceases rather quickly. Sterile dry dressings are applied until the oozing stops, after which the entire face is dressed firmly with Telfa dressings, and the patient is sent on his way. In that few minutes' period between the brushing and the bandaging, there is a considerable but tolerable burning sensation.

The patient is instructed to remove the bandage and dressings 24 hours later at home and to expect that by then the bandage will be bloodstained, the face swollen considerably, and that serum may exude for an hour or two, then dry into crusts which will begin to drop off in six or seven days. A prescription for Empirin with codeine is supplied, should headache develop. The face may be washed at any time after the first 24 hours but should be dried by blotting rather than by rubbing with a towel. When the crusts have all dropped off (usually about 10 days to 2 weeks), women may use their cosmetics and men their electric razors and resume their occupations.

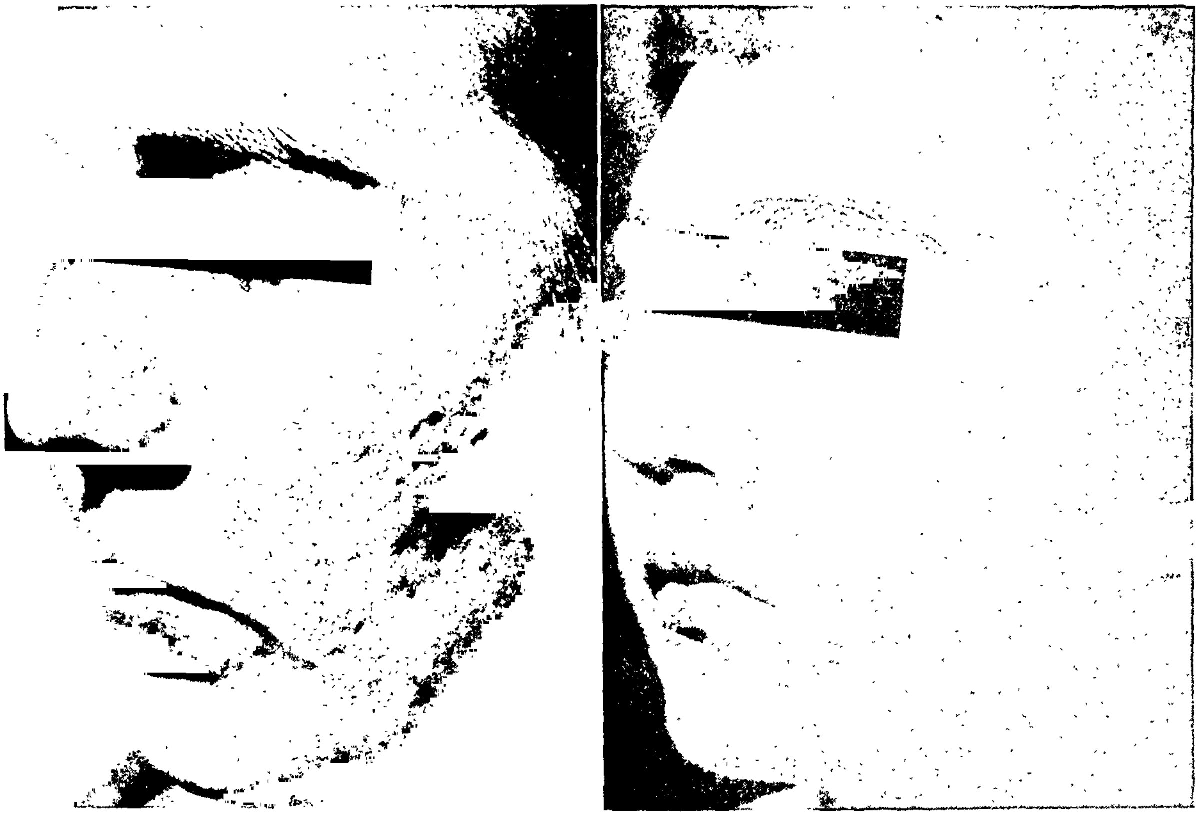

Fig. 3.—*Left*, appearance of skin before dermabrasion and, *right*, after, in same patient.

Sometimes vellus hairs prevent the crusts from falling; in such cases, the application of a petrolatum dressing will remove the crust. Most patients find the experience to be much less formidable than they had expected. Some, of course, find it traumatic, the number of patients, in our experience, being almost directly proportional to the amount of admonition and postoperative instructions issued to them.

Complications

The complications are infrequent and are usually unimportant. Impetigo, readily controlled with antibiotic agents, may occur in the first two weeks. Milia may appear weeks later; emptying them hastens their involution, but most disappear in time. More rarely, postoperative erythema may persist for several months instead of for the usual three or four weeks. This may be due to excessive refrigerations, overexposure or premature exposure to sunlight after the operation, or overly vigorous cleansing. In unusual cases and particularly in dark-complexioned persons, hyperpigmentation, especially at the edges of the abraded area, develops and may persist for months. This is an unhappy experience because the patient who is seeking relief from a cosmetic defect is disturbed by another. The appearance of a postoperative eczematous patch has been reported as a complication of dermabrasion; we have not observed it. In one instance, we have observed the development of two small hypertrophic scars, one of which was treated, the other not, and both disappeared. Though we have heard of a few instances of true keloids developing after abrasion, we ourselves have not observed any.

Results

The results from dermabrasion cannot be assessed in precise mathematical terms. Unfortunately, in the beginning, the limitations of the treatment were not fully realized, and inevitably the technique was both abused and misused. Most unfortunate were the unduly glowing reports that appeared in some lay publications, so that in far too many instances the outcome was disappointing.

Since then, planed skin has been subjected to thorough clinical and microscopic studies to determine the effects from refrigeration and the physiological processes of epithelial regeneration.[4] Much thought has also been given to the psychological aspects of the problem.

The results from treatment depend a good deal upon the shape and depth of the scars and also upon the skill of the operator. Superficial flat-surfaced scars with abrupt edges respond exceptionally well to treatment; the wide, ill-defined, confluent scars that impart an undulating appearance to the skin, less so; the deep-pitted, so-called *ice-pick* type of scars, practically not at all; and, of course, widened or patulous pores cannot be narrowed. The latter type of skin, i. e., the leathery skin with deeply pitted, narrow scars interspersed with innumerable wide pores, occurs all too frequently and often produces the most severe cosmetic defect,

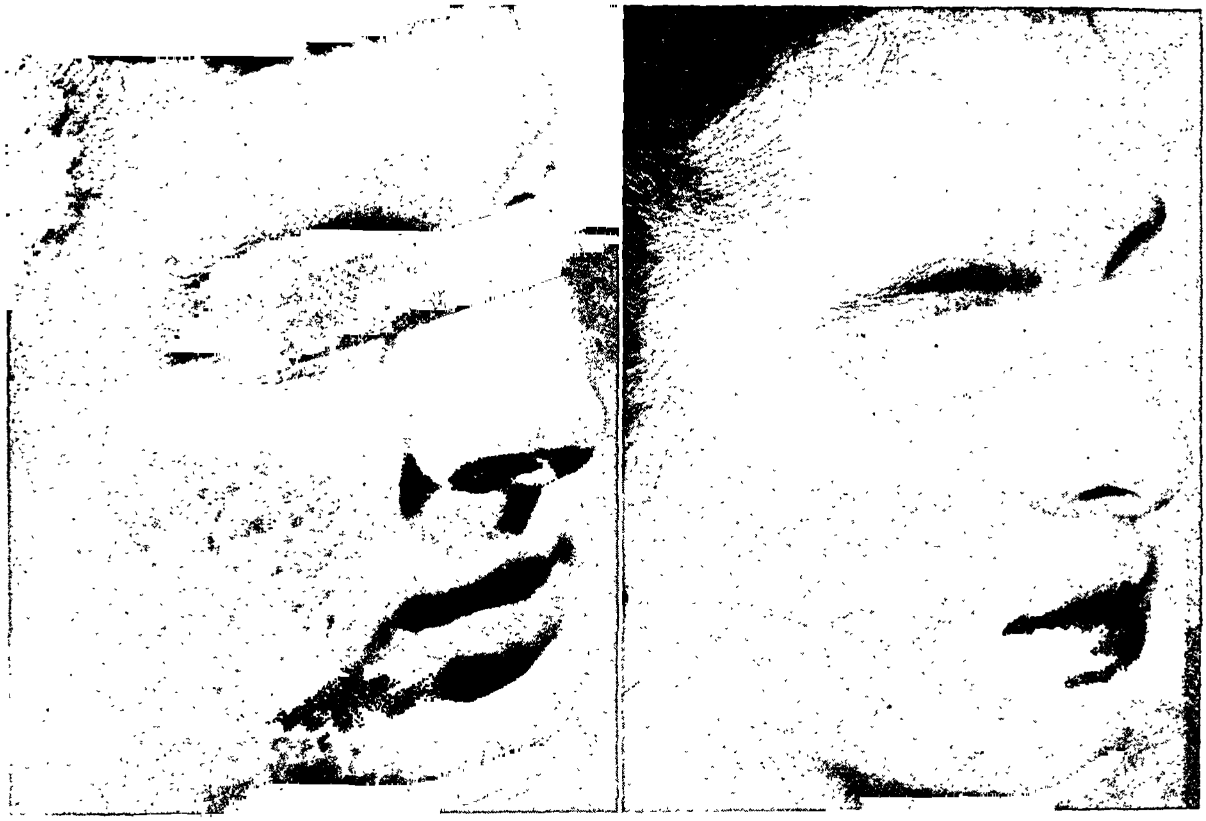

Fig. 4.—*Left,* scars seen before dermabrasion and, *right,* improvement seen afterward, in same patient.

so that, unfortunately, the person with the greatest need for help obtains the least amount of benefit from dermabrasion.

Scars on the cheeks and, to a lesser degree, scars on the forehead and temples respond best to dermabrasion because of the rich supply in these areas of pilosebaceous units from which regeneration is stimulated. Scars on the chest, back, shoulders, and neck respond poorly. Scars of recent origin appear to respond better than do old scars. The age of the patient is not important, and the presence of a few acne lesions need not deter one from treatment. It is best to abrade all scars at one time rather than small areas at spaced intervals.

Aside from the aforementioned complications which occur rarely, the procedure is a safe one in careful hands. If care is given to the selection of the person to be treated, as well as to the shape and depth of the scars, the procedure can be a satisfying one for all concerned. Practically all patients benefit from the treatment to some degree (fig. 2, 3, and 4); not all benefit as much as they would like. The emotionally disturbed person who attributes his or her unhappiness to the acne scars is certain to be displeased with the result—as is the perfectionist with barely noticeable scars who wants to have the skin of a baby. The emotionally mature, reasonably intelligent person who will accept improvement short of "cure" is the most satisfactory patient. Almost all of them, however, show some measure of anxiety, fear, and uncertainty when they come to consult about the procedure. It is well, therefore, to discuss the matter with the patient in the presence of a relative. The technique and the postoperative course should be fully described, and the likelihood that the results may fall short of the patient's expectations should be mentioned several times. It is tempting fate to try to foretell the amount, percentage-wise, of improvement to be expected from treatment. In some cases it may be desirable to repeat the treatment once or twice after an interval of eight months or more. It is well, too, for the patient to consider all the factors for several days before deciding to undergo the treatment. It is highly desirable that a preoperative photograph be taken in every case and made a part of the record. The degree of improvement may then be appreciated by surgeon and patient alike.

Conclusion

A realistic appraisal of the method would indicate that dermabrasion for the improvement of acne scars can be a rewarding experience for both the physician and the patient, provided the patient is selected with great care and the scars are assessed critically with regard to their shape, depth, and location and provided also that the patient will accept improvement that is short of a perfect result. In such cases, the vast majority of patients are pleased with the results, often more so than the physicians. The cosmetic improvement and, in particular, the improved well-being of the patient are such as to indicate that physicians take too lightly the importance of acne scars to the patient. We are constantly impressed by the numbers of mature men and women who seek the treatment and assure us that even a slight amount of treatment would be most welcome and worth the effort. On the other hand, it would be folly to undertake dermabrasion in order to cure emotional disturbances occasioned by acne scars. Unfortunately, the person with a leathery, pitted, wide-pore type of skin, most anxious for and most in need of help, gets practically none from dermabrasion.

104 S. Michigan Ave. (3) (Dr. Rattner).

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THE CERVICAL MUCUS DURING OVULATION.—Spinnbarkeit is a characteristic of the cervical mucus which, as its name signifies, indicates the ability of the mucus to be drawn out into a very fine thread after having been removed from the cervix with a glass cannula. The material is blown out onto a glass slide and a coverslip placed on it. By lifting the coverslip off the slide several times the length of the thread of mucus which is formed can be measured without difficulty and the average length can be obtained. At the time of maximal production of cervical mucus, which closely parallels the time of ovulation and which also closely parallels the time of maximal estrogen production by the ovarian follicles, the spinnbarkeit reaches a length of from 10 to 20 cm.; at other times, particularly just before ovulation, it will be impossible to draw out a thread longer than 1, or 2 cm. at the most.—G. C. Douglas, M.D., Is There a Routine Cervical Smear? *The American Surgeon,* October, 1959.

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LIFE IN A TEST TUBE AND ELSEWHERE

A few weeks ago, on Nov. 24 to be exact, nine eminent dentists from this country and abroad sat on a panel at the University of Chicago to review certain facts known by members of their guild and to exchange opinions on the origin of life. This rare and deservedly widely publicized occasion was the 100th anniversary of Charles Darwin's book, "The Origin of Species." A scientifically minded audience from far and near filled Mandel Hall, hoping no doubt to learn from where and how they came to be there.

The panelists probably expressed their biochemical, astronomical, and genetic ideas in terms as simple as possible. Still the imagination of the audience at times was strained, and the energy expended by the panelists themselves apparently was such that the chairman considered it advisable to have a short recess in the middle of the session for everyone to recuperate. Perhaps when evolution has advanced far more than it has at present, the average homo sapiens will be more at home with such terms as "billions of years ago" and "the hundred thousand million billion stars." The panelists probably had digested *in toto* many technical documents and had endured long periods of observation and experimentation to come forth with these inordinate figures. Nevertheless, they did point out rather simply that Darwinian evolution is not a theory any more, but a fact, and that long, long ago some of the first organic compounds were of such kinds that they could readily be transformed into parts of living things.

To the question of what life is, a panelist said that the most fundamental property distinguishing a living thing and that can be used to define life is its ability to form copies of itself. "We call it reproduction but the copies must even include innovations which we call mutations, that distinguish the given living thing from its parents. It is this property of not merely reproducing itself by even reproducing its types that has inevitably led the first multiplying object to go through the three, four, or five billion years of gradual evolution with which all present day living things, including ourselves, have gradually taken shape under the directing influence of natural selection."

Another panelist said that from the standpoint of the composition of living things, when we reach a point where we all agree that it is living, we always find three components at that level. "We find proteins, nucleic acids, and some sort of energy source; the third component is the necessary one, because the system of organization is the essence of the living cells. We know that the living thing is essentially unstable and so these components are not unique characteristics of living things. Other actions happen too, but when we find life we find all of these three components there."

So far as this pre-Darwinian idea is concerned, one speaks of viruses. The virus is, in certain manifestations, difficult to define as being either living or nonliving. In their isolated stage, viruses do not show any source of energy, for example, and from that standpoint they are nonliving. When one introduces a virus into the host cell, it replicates. It uses the machinery of the host cell. Under these circumstances, it is able to communicate and replicate. One might say, therefore, that under these circumstances not the virus but the virus and host cell together form a living system; but this is no answer to the question of what is living or nonliving. The exchange of opinions continued, but there was no agreement on an exhaustive definition of what life is.

Nucleic acid was given further consideration, particularly the large multicolored model (on a stand) of the nucleic acid molecule. The tendency at present, it seems, is to identify desoxyribose nucleic acid, one of the two types of nucleic acid, with the genetic material itself, that is, the genes. Ribonucleic acid, the other type of nucleic acid, is present in the cytoplasm of cells, and the two types are distinguished by the nature of the sugar they have in them.

The Urey-Miller experiment is widely known to scientists and its importance is appreciated, but it was news to some and perhaps to many of those in Mandel Hall. Prof. Harold C. Urey conceived a hypothesis, and Dr. Stanley Miller of the University of Chicago a few years ago put it to the test and proved it to be true. Miller subjected to electrical discharges a mixture of hydrogen and water vapor, ammonia, and methane, and he thus produced a number of amino acids, which are the building blocks of proteins, which are the building blocks of living matter.

Near the close of the two-hour session written questions were sent up from the audience, and one that the chairman preferred was "Please poll the panel for their opinion of the estimate that life can be created in test tubes in 1,000 years." One panelist said that in terms of a replicating and mutating macromolecule, it is quite possible in 1,000 years; another thought that perhaps we will make it in 500 years; another was confident that it would be solved during his lifetime (perhaps 20 or 30 years); and another estimated that it would be done before the end of the century. Then, perhaps, came a shock, when a geneticist said, "My answer is that ... defining life as I do, the most primitive forms of things which deserve to be called living have already been made in the test tube."

Four other panels participated in this great celebration discussing various phases of evolution, and if they were similarly adept it would seem that more favorable mutations must be awaited before scientists agree on many of these questions.

ARE YOU AWARE?

The warning to "beware" or be "on the alert" will cause the thoughtful physician to slow his pace and possibly ponder the reason for the admonition. Should the unsuspecting physician be inattentive to the remonstrance, in some instances, it may cause him to contemplate seriously the consequences.

Over the generations as well as over the centuries of human activity, mental capacity for planning and mental capacity for initiating fortunately persist. If Aristotle or Plato could be exposed to the environment of 1959 in medicine, physics, radiobiology, or enzyme chemistry, to mention only a few scientific disciplines, there is little doubt but that either would be sufficiently skilled to be a leader in his field of endeavor or a professor in his department in the university. If these men were now in such positions of responsibility, the influence of their thoughts and actions undoubtedly would be profound. But we are now in the waning hours of 1959. Looking to 1960, we should take heed of the past and be on the alert for continued change in the future. Those physicians who have been aware must have appreciated the effectual attempts at integration of the diverse activities at the American Medical Association headquarters, under the authority of the Board of Trustees and the House of Delegates.

New leadership in several of the Divisions and sympathetic but forthright and aggressive guidance at the helm are welcome attributes at 535 N. Dearborn St. Each participant is dedicated to the premise that the future course of events for American medicine is critical for all interested parties. As we look ahead we see that the impetus makes it inevitable that the evolution will continue slowly and surely in the Association that represents the physicians of this country. A new facade is on the building, there are new faces in the offices, and new philosophies are widely apparent. We are convinced that the transformation and metamorphosis will be a tremendous force for the good in the immediate future as well as for many years hence in American medicine.

JOURNAL INDEX

The index to volume 171 of THE JOURNAL will appear in the Jan. 9, 1960, issue. Those who wish extra copies of the index may receive them, without charge, on request to the Circulation and Records Department, American Medical Association, 535 N. Dearborn St., Chicago 10.

ORGANIZATION SECTION

SUMMARY OF THE DALLAS MEETING

Freedom of choice of physician, relations between physicians and hospitals, a scholarship program for deserving medical students, and relative value studies of medical services were among the major subjects acted on by the House of Delegates at the American Medical Association's 13th Clinical Meeting held Dec. 1-4 in Dallas.

Dr. Chesley M. Martin of Elgin, Okla., was named as the 1959 General Practitioner of the Year for his outstanding contributions to the health and civic affairs of his home community. Dr. Martin, who has practiced in Elgin for the past 44 years, was the 13th recipient of the annual award and the first Oklahoman to be so honored.

Speaking at the Tuesday opening session of the House, Dr. Louis M. Orr of Orlando, Fla., A. M. A. President, urged the nation's physicians to take a more active interest in the whole area of politics, public affairs, and community life. Dr. Orr also asked physicians and medical societies to do a more effective job of telling medicine's positive story, adding that "if more people knew more about the things we support and encourage, they would listen to us much more carefully about those occasional things that we oppose."

Two nationally known political leaders from Texas also addressed the Tuesday morning session. Sen. Lyndon B. Johnson, majority leader in the U. S. Senate, called for a "politics of unity" which will enable Americans to exert strength and determination in an effort to create a world in which all men can be free. Speaker of the U. S. House of Representatives Sam Rayburn urged greater attention to the task of educating young people in the principles of American government and giving them a desire to perpetuate it.

Total registration through Thursday, with half a day of the meeting still remaining, had reached 4,727, including 2,742 physicians.

Freedom of Choice

In considering four resolutions which in various ways would have changed or replaced the statements on freedom of choice of physicians which the House adopted in June, 1959, when acting on the recommendations in the report of the Commission on Medical Care Plans, the House reaffirmed the following two statements approved in Atlantic City:

1. "The American Medical Association believes that free choice of physician is the right of every individual and one which he should be free to exercise as he chooses."
2. "Each individual should be accorded the privilege to select and change his physician at will or to select his preferred system of medical care, and the American Medical Association vigorously supports the right of the individual to choose between these alternatives."

However, in order to clarify and strengthen its position on the issue of freedom of choice of physician, the House also adopted this additional statement which was submitted as a substitute amendment on the floor of the House:

3. "Lest there be any misinterpretation, we state unequivocally that the American Medical Association firmly subscribes to freedom of choice of physician and free competition among physicians as being prerequisites to optimal medical care. The benefits of any system which provides medical care must be judged on the degree to which it allows of, or abridges, such freedom of choice and such competition."

Near the conclusion of the discussion it was emphasized that the amendment was intended to strengthen the position stated last June, not to modify or retract such position.

Physician-Hospital Relations

The House received 12 resolutions on the subject of relationships between physicians and hospitals. To resolve any doubt about its position, the House did not act on any of the resolutions but instead reaffirmed the 1951 "Guides for Conduct of Physicians in Relationships with Institutions." It also declared that "all subsequent or inconsistent actions are considered superceded."

It was recommended and accepted also that (1) the House of Delegates acknowledge the need to strengthen relationships with hospitals by action at state and local levels, (2) the Board of Trustees of the Association continue to maintain liaison with the Board of Trustees of the American Hospital Association, and (3) the Council on Medical Service review this entire problem to ascertain if there have been actions inconsistent with the 1951 Guides.

Those Guides summarize the following general principles as a basis for adjusting controversies:

"1. A physician should not dispose of his professional attainments or services to any hospital, corporation, or lay body by whatever name called or however organized under terms or conditions which permit the sale of the services of that physician by such agency for a fee.

"2. Where a hospital is not selling the services of a physician, the financial arrangement if any between the hospital and the physician properly may be placed on any mutually satisfactory basis. This refers to the remuneration of a physician for teaching or research or charitable services or the like. Corporations or other lay bodies properly may provide such services and employ or otherwise engage doctors for those purposes.

"3. The practice of anesthesiology, pathology, physical medicine, and radiology are an integral part of the practice of medicine in the same category as the practice of surgery, internal medicine, or any other designated field of medicine."

Scholarship Program

To help meet the need for an increased number of physicians in the future, the House approved the creation of a special study committee which was asked to:

1. Present a scholarship program, its development, administration and the role of the American Medical Association in fulfilling it.
2. Ascertain the maximum to which medical schools could expand their student enrollment and maintain the high quality of medical education.
3. Ascertain what universities can support new medical schools with qualified students and sufficient clinical material for teaching—either on a two-year or a full four-year basis.
4. Investigate the securing of competent medical faculties.
5. Investigate financing of expansion of existing facilities and establishment of new medical schools.
6. Investigate financing of medical education in order to ascertain the most economical methods for procuring the highest quality of medical training.
7. Develop methods of recruiting well-qualified students to undertake the study of medicine.
8. Investigate the possibility of relaxing rigid geographical restrictions of medical schools for the admission of students.

The House urged that the special committee be implemented with adequate funds and staff promptly so that it may make an initial report by June, 1960.

Relative Value Studies

Reaffirming a previous policy statement, the House approved in principle the conducting of relative value studies by each state medical society, rather than a nationwide study or a series of regional studies by the A. M. A. The House also reiterated its authorization for the Committee on Medical Practices to inform each state medical association, through regional or other meetings, of the purpose, scope and objectives of such studies, the steps to be followed in conducting studies, the problems which may be encountered, and the manner in which the results can be applied.

The House recognized, however, that some state medical societies either are not interested in relative value studies or are actively opposed to them. It pointed out that some state medical associations fear that the regional conferences of the Committee on Medical Practices will put pressure on them to carry out such studies and that this will result in the adoption of "fixed fees."

Since the regional conferences are educational in nature, the House affirmed that: It is the obligation of each state or county medical association to accept or reject the idea of a study in its area.

The House was aware that this subject matter remains controversial. However, it commended the Committee on Medical Practices for its effort to carry out the instructions of the House, and it urged the committee to continue its educational work.

Miscellaneous Actions

In considering 44 resolutions and a large volume of annual, supplementary and special reports, the House also was informed that the A. M. A. Board of Trustees has appointed a liaison committee to meet with a similar committee of the American Osteopathic Association to consider matters of common concern; emphasized that local medical societies should insure that no member violates ethical traditions as they relate to ownership of pharmacies or stock in pharmaceutical companies; approved the plan of the Committee on Medical Rating of Physical Impairment to publish its new guide on the cardiovascular system in THE JOURNAL; recommended that Association councils and committees, whenever feasible, hold their meetings in the remodeled Chicago headquarters; called for investigation of the need, desirability, and feasibility of establishing a home for aged and retired physicians; commended Dr. F. S. Crockett, retiring chairman of the Council on Rural Health, for his many years of devoted duty; urged active promotion and careful study of the newly developed "Guides for Medical Care in Nursing Homes and Related Facilities"; suggested that fees for consultative examinations under programs of the Bureau of Old Age and Survivors Insurance should be adjudicated directly between the state medical society and the state agency involved; registered a strong protest to the Veterans Administration and urged strict screening of non-service-connected disability patients admitted to government hospitals; reiterated the Association's support of the Blue Shield concept and directed the Council on Medical Service to submit at the June, 1960, meeting its recommendations concerning a policy statement on A. M. A. relationship with Blue Shield plans; suggested that S. J. Res. 41, a bill which would institute a separate program of international medical research, be delayed until an over-all assessment can be made of proposals now before Congress dealing with domestic and international medical research; endorsed the program of the Educational Council for Foreign Medical Graduates but also urged that judicious consideration be given to local problems involved in the July 1, 1960, deadline for certification of foreign graduates; urged that medical schools include in their curriculums a course on the social, political, and economic aspects of medicine; declared that the threat of nuclear warfare has imposed a tremendous responsibility on the medical profession, which must be prepared to assume a critically important role in such an event; suggested that the A. M. A. make available to school libraries information and literature showing the advantages of private medical care and the American free enterprise system; stated that examinations to determine the physical and mental fitness of aircraft crew members should be made by doctors of medicine with special knowledge and proficiency in certain techniques; urged the American people to receive proper tetanus toxoid, original and booster, and other immunizations as indicated from their physicians, and called on A. M. A. members to cooperate in an educational program on tetanus immunization; recommended that all state and county medical societies establish programs for the inspection and testing of fluoroscopes and roentgenographic equipment; approved the Speaker's proposal that the opening session of the House, at the Interim Meeting, be moved from Tuesday morning to Monday morning, with the reference committees meeting on Tuesday and the House reconvening on Wednesday afternoon; called on each individual physician to wage "a vigorous, dynamic, and uncompromising fight" against the Forand type of legislation; urged state and local medical societies and individual physicians to implement the A. M. A. program for recruitment of high-grade medical students; changed the title of the Section on Surgery, General and Abdominal, to the Section on General Surgery; accepted with appreciation a $2,500 contribution by Smith Kline and French Laboratories toward establishment of a suitable award honoring the name of Dr. Thomas G. Hull, retiring secretary of the Council on Scientific Assembly; and reaffirmed the "Suggested Guides to Relations Between Medical Societies and Voluntary Health Agencies," which were adopted at the December, 1957, meeting in Philadelphia.

At the Tuesday opening session, six state medical societies presented nearly $250,000 to the American Medical Education Foundation. The moneys accepted by Dr. George F. Lull, president of AMEF, were: California, $156,562; Indiana, $35,570; New York, $19,546; Utah, $10,355; New Jersey, $10,000; and Arizona, $9,263.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

SUPPLEMENTARY LIST—CORRECTIONS

In the annual Internship and Residency Number of THE JOURNAL, *Oct. 10, 1959, incomplete or inaccurate data were presented. The correct entries are as follows.*

In addition to publishing the Directory of Approved Internships and Residencies in the Internship and Residency Number annually, it is planned to publish newly approved programs on a quarterly basis. The first such quarterly list is scheduled for January, 1960.

Approved Residencies and Fellowships

INTERNSHIPS

Name of Hospital and Location	Control	Total Beds	Number of Patients Admitted	Outpatient Service	Autopsy Percentage	Length of Program (Months)	Affiliated Service	Beginning Stipend (Month)	Number and Type of Internships	Code Number
Baltimore City Hospitals +[1-3-4]-X38-x37.......	City	1,140	12,140	Req	73	12	157	125FM	12 Rotating General	23711
4940 Eastern Ave., Baltimore 24, Md.									10 Straight Medicine	23732
									6 Straight Surgery	23733
									3 Straight Pediatrics	23734
									1 Straight Pathology	23736
									2 Mixed (Med.-Ped.)	23753
									2 Mixed (Ped.-Med.)	23754
t Auburn Hospital +[1-3]-x40.	NPCorp	248	8,235	Req	56	12	288	120FM	4 Mixed (Med.-Surg.-Ped.)	26923
0 Mt. Auburn St., Cambridge 38, Mass.										
s Hospital +[1-3]-x63-64.....................	NPCorp	293	11,095	Req	39	12	No	250FM	10 Rotating General	87711
road St. and Club Blvd., Durham, N C.									3 Rot. Med. Major	87712
									2 Straight Medicine	87732
									1 Straight Ob.-Gyn.	87735
e Island Hospital +[1-3-4]...................	NPCorp	659	19,395	Req	41	12-24	250	100FM	18 Rotating General	67711
93 Eddy St., Providence 2, R. I.										

Affiliations as Referred to in Column Headed:
"Affiliated Service"

288. Boston Lying-In Hospital, Boston

ANESTHESIOLOGY

Residency programs in the following hospitals have been approved for TWO years of training by the Council and the American Board of Anesthesiology, through the Residency Review Committee for Anesthesiology.

Name of Hospital	Location	Chief of Service	Total Anesthetics	Inhalation Anesthetics	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Veterans Admin. Hospital [1-3-153].........................	Hines, Ill.	M. Sadove....................	3,080	1,739	4	7	270
University Hospital [1-3]...................................	Baltimore	M. Helrich....................	7,914	5,104	6	14	275
St. Joseph's Hospital.........................	Far Rockaway, N. Y.	R H. Berman-J. Turbin......	...	...	..	..	...

DERMATOLOGY

Name of Hospital	Location	Chief of Service	Inpatients Treated	Outpatient Visits	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
University Hospital [1-3]...................................	Baltimore	H M. Robinson Jr.	250	10,733	2	6	3	200

GENERAL PRACTICE

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
University Hospital [1-3]...................................	Baltimore	G. Entwisle..............	Incl. in Int. Med.		2	3	2	200

INTERNAL MEDICINE

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
Baltimore City Hospitals [1-3]............................	Baltimore	G. S. Mirick...............	1,591	138	4	9	3	200
University Hospital [1-3]...................................	Baltimore	T. E. Woodward..........	3,597	198	19	33	3	200
Methodist Hospital [1-3].................................	Minneapolis	D. R. Hastings............	2,695	77	1	1	1	200
St. Luke's Hospital [1-3]...........................	New York City	T. B. Van Itallie..........	3,120	119	8	15	3	100
Baptist Memorial Hospital [1-3].....................	Memphis, Tenn.	P. Milnor Jr.	10,835	124	2	5	1	325

NEUROLOGICAL SURGERY

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
Medical College of Georgia Hospitals			...	..	..	..	4	...
Eugene Talmadge Hospital [1-3]	Augusta, Ga.	G. Smith	343	14	1	5	..	250
University Hospital [1-3]	Augusta, Ga.	P. Nichols	628	12	1	1	..	200
Veterans Admin. Hospital [1-3]	Augusta, Ga.		...	..	..	..	..	...
Johns Hopkins Hospital [1-3]	Baltimore	A. E. Walker	790	25	2	6	4	25
Baltimore City Hospitals [1-3]	Baltimore	J. D. McQueen	233	10	..	1	..	225
University Hospital [1-3]	Baltimore	J. G. Arnold	872	48	1	6	4	200

NEUROLOGY

Residency programs in the following hospitals have been approved for THREE years of training by the Council and the American Board of Psychiatry and Neurology, through the Residency Review Committee for Psychiatry and Neurology. (Applicants intending to qualify for examination by the American Board of Psychiatry and Neurology, Inc., should refer to the Board requirements that the candidate have had at least two of the three years of his training in a program or programs approved at the two or three year level.)

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Baltimore City Hospitals [1-3]	Baltimore	J. W. Magladery	741	56	2	3	200
University Hospital [1-3]	Baltimore	C. Van Buskirk	207	15	2	4	200
University of Vermont College of Medicine Affiliated Hospitals		G. A. Schumacher	420	15	1	3	330
De Goesbriand Memorial Hospital [1-3]	Burlington, Vt.	H. Martin	...	..	..	..	...
Mary Fletcher Hospital [1-3]	Burlington, Vt.	G. A. Schumacher	...	..	..	..	...

OBSTETRICS—GYNECOLOGY

Name of Hospital	Location	Chief of Service	Residencies Approved	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
Baltimore City Hospitals [1-3]	Baltimore	P. E. Molumphy	OBG	6,603	8	6	18	3	125
University Hospital [1-3]	Baltimore	A. L. Haskins	OBG	4,918	9	6	15	3	200

OPHTHALMOLOGY

Name of Hospital	Location	Chief of Service	Inpatients Treated	Outpatient Visits	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
Cleveland Metropolitan General Hospital [1-3]	Cleveland	R. J. Nicholl	115	4,900	1	4	3	150
St. Luke's Hospital [1-3]	Cleveland	G. T. Schwarz	411	4,759	..	..	..	200

ORTHOPEDIC SURGERY

Type of training acceptable to Board: A—Adult Orthopedics; C—Children's Orthopedics; F—Fractures. Residency programs in the following hospitals have been approved by the Council and the American Board of Orthopedic Surgery, through the Residency Review Committee for Orthopedic Surgery, as offering acceptable training in adult orthopedics, children's orthopedics, and fractures. Training in the basic sciences is given either as an integral part of these services or as a separate course. Services collaborating in an integral plan of training are designated by a program number.

Residents completing their training in these hospitals are eligible for full certification by the American Board of Orthopedic Surgery, including children's orthopedic surgery.

Name of Hospital	Location	Chief of Service	Type of Training	Program Identification	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Baltimore City Hospitals [1-3]	Baltimore	R. A. Robinson	AF	57	332	3	..	1	225
University Hospital [1-3]	Baltimore	A. F. Voshell	AF	88	349	1	1	3	200

OTOLARYNGOLOGY

Name of Hospital	Location	Chief of Service	Inpatients Treated	Outpatients Visits	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
University Hospital [1-3]	Baltimore	C. L. Blanchard	341	4,817	2	6	250
University of Kansas Medical Center [1-3]	Kansas City, Kan.	G. O. Proud	831	13,375	1	4	125
Veterans Admin. Hospital [1-3-20]	Kansas City, Mo.	H. A. Knauff	252	3	..	..	271

PATHOLOGY

Name of Hospital	Location	Chief of Service	Number of Autopsies	Total Number of Laboratory Examinations	Number of Surgical Specimens	Number Examined Microscopically	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
San Joaquin General Hospital [1]	Stockton, Calif.	H. J. Schneider	432	148,299	2,722	2,241	1	1	3[a]	260
Veterans Admin. Hospital [1-3-161]	Hines, Ill.	M. Rubnitz	625	619,936	3,878	3,693	4	10	4[p]	270
Baltimore City Hospitals [1-3]	Baltimore	A. D. Pollack	479	165,829	2,958	2,958	2	5	3[p]	125
University Hospital [1-3]	Baltimore	H. J. Firminger	461	455,576	7,630	7,630	2	8	4[p]	350
Holy Cross Hospital [1-3]	Salt Lake City	C. McNeil	132	123,654	5,930	5,112	1	1	4[p]	275

PEDIATRICS

Residency programs in the following hospitals have been approved by the Council, the American Academy of Pediatrics and the American Board of Pediatrics, through the Residency Review Committee for Pediatrics, as offering full training in the specialty: (i. e., TWO or more years).

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Duval Medical Center [1-3]	Jacksonville, Fla.	J. K. David Jr.	518	18	2	4	200
St. Vincent's Hospital [3]	Jacksonville, Fla.	H. A. Carithers	2,668	15	1	2	325
Baltimore City Hospitals [1-3]	Baltimore	H. E. Harrison	1,786	185	3	9	125
University Hospital [1-3]	Baltimore	J. E. Bradley	1,373	87	3	7	200

PHYSICAL MEDICINE AND REHABILITATION

Name of Hospital	Location	Chief of Service	Inpatients Treated	Number of Treatments	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
Bellevue Hospital Center [illegible] ty	New York City	H. Rusk	17,122	111,873	..	15	3	145
[illegible] [1-3]	New York City	A. S. Russek	2,086	22,856	..	..	..	80

PSYCHIATRY

Residency programs in the following hospitals have been approved for THREE years of training by the Council and the American Board of Psychiatry and Neurology, through the Residency Review Committee for Psychiatry and Neurology.

Name of Hospital	Location	Chief of Service	Program Identification	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Veterans Admin. Hospital [1-3-154]	Hines, Ill.	L. Jensen	25	729	4	5	15	270
University Hospital [1-3]	Baltimore	J. E. Finesinger	..	503	1	7	22	275

PULMONARY DISEASE

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Essex County Sanatorium [1-3]	Verona, N. J.	I. Ocheret	662	28	2	4	577.83

RADIOLOGY

Name of Hospital	Location	Chief of Service	Number of X-Ray Examinations	Number of Radium Treatments	Number of Deep X-Ray Treatments	Number of Superficial X-Ray Treatments	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Veterans Admin. Hospital [1-3-148]	Hines, Ill.	F. Hussey	69,657	698	11,079	346	6	12	270
Baltimore City Hospitals [1-3]	Baltimore	J. De Carlo	32,426	7	810	137	1	4	125
[illegible]	Baltimore	J. M. Dennis	59,836	148	10,755	...	2	7	250
[illegible] ed Hospitals	Dallas, Texas	F. Bonte	48,686	57	2,475	775	2	7	150

SURGERY

Residency programs in the following hospitals have been approved by the Council, the American Board of Surgery and the American College of Surgeons, through the Conference Committee on Graduate Training in Surgery, for FOUR OR MORE years of training, designed to qualify the trainee for examination by the American Board of Surgery as a Group I candidate.

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Baltimore City Hospitals [1-3]	Baltimore	M. M. Ravitch	1,044	59	6	17	125
University Hospital [1-3]	Baltimore	R. W. Buxton	2,999	72	10	23	200

Residency programs in the following hospitals are approved by the Council as offering satisfactory training of ONE or TWO years' duration in preparation for residency training in the surgical specialties only. Applicants intending to qualify for examination by the American Board of Surgery should refer to the lists of approved services on pages 774 through 781 (Surgical Residencies, J. A. M. A. 156:432, Sept. 25, 1954).

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
St. Bernard's Hospital	Chicago	E. A. Balcer	...	..	..	..	...

THORACIC SURGERY

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
University Hospital [1-3]	Baltimore	R. A. Cowley	277	16	3	7	2	200

UROLOGY

Name of Hospital	Location	Chief of Service	Inpatients Treated	Autopsies	First-year Residencies Offered *	Total Residencies Offered *	Beginning Stipend (Month)
Indiana University Medical Center [431]							
Indiana University Medical Center Hospital [1]	Indianapolis	R. A. Garrett	325	6	2	8	225
Marion County General Hospital [1-3]	Indianapolis	R. D. Howell	370	11	1	4	210
Veterans Admin. Hospital [1-3]	Indianapolis	R. A. Garrett	624	177	..	..	271
Methodist Hospital [1]	Indianapolis	M. H. Nourse	2,225	8	1	2	278
University Hospital [1-3]	Baltimore	J. D. Young Jr.	851	15	2	6	200

NUMERICAL AND OTHER REFERENCES

289. City Hospital at Elmhurst, Goldwater Memorial Hospital, Institute of Physical Medicine & Rehabilitation, Montefiore Hospital, St. Barnabas Hospital, St. Vincent's Hospital, University Hospital, Veterans Admin. Hospital (Manhattan), New York City; Grasslands Hospital, Valhalla, N. Y., New York State Rehabilitation Hospital, West Haverstraw, N. Y.

431. Methodist Hospital, Indianapolis.

APPROVED RESIDENCY TRAINING PROGRAMS

Name	Location	Approved Residencies
Orange County General Hospital ★	Orange, Calif.	Int. Med., Rad.
Palo Alto-Stanford Hospital Center ★	Palo Alto, Calif.	Anes., Derm., Int. Med., Neur., Ob.-Gyn., Otol., Ortho. Surg., Path., Ped., Psych., Rad., Surg.
Methodist Hospital ★	Minneapolis	Int. Med.
St. Barnabas hospital	Minneapolis	Int. Med., Ob.-Gyn., Path., Surg.
Christ Hospital ★	Cincinnati	Anes., Gen'l Pract., Int. Med., Neuro. Surg., Plas. Surg., Surg.
State of Connecticut Vet. Home and Hospital	Rocky Hill, Conn.	Phys. Med.
Laurel Heights Hospital	Shelton, Conn.	Pul. Dis.
Stamford Hospital ★	Stamford, Conn.	Path., Surg.
Charlotte Hungerford Hospital	Torrington, Conn.	Gen'l Pract.
St. Mary's Hospital ★	Waterbury, Conn.	Anes., Int. Med., Path., Rad., Surg.
Waterbury Hospital ★	Waterbury, Conn.	Int. Med., Path., Ped., Rad., Surg., Urol.
State of Delawar	Dover Del.	Pub. Health
Delaware State	Del.	Psych.
Alfred I. Du Pon	Del.	Ortho. Surg.
Delaware Hospital ★	Wilmington, Del.	Card. Dis., Int. Med., Ob.-Gyn., Path., Ped., Rad., Surg., Urol.
Memorial Hospital ★	Wilmington, Del.	Int. Med., Path., Surg.
Wilmington General Hospital ★	Wilmington, Del.	Gen'l Pract., Int. Med., Ob.-Gyn., Path.
Armed Forces Institute of Pathology	Washington, D. C.	Path.
Army Medical Center (Walter Reed Army Hospital) ★	Washington, D. C.	Allergy, Anes., Card. Dis., Derm., Gastro., Int. Med., Neur., Neuro. Surg. Ob-Gyn., Ophth., Ortho. Surg., Otol., Path., Ped., Phys. Med., Psych., Rad., Surg., Thor. Surg., Urol.
Children's Hospital	Washington, D. C.	Neuro. Surg., Path., Ped. Allergy, Ped., Psych., Surg
Columbia Hospital For Women and Lying-In Asylum	Washington, D. C.	Ob.-Gyn.
District of Columbia General Hospital ★	Washington, D. C.	Anes., Int. Med., Neur., Neuro. Surg., Ob.-Gyn., Ophth., Ortho. Surg., Path., Ped., Phys. Med., Psych., Pul. Dis., Rad., Surg., Urol.
Doctors Hospital ★	Washington, D. C.	Int. Med., Ob.-Gyn., Path., Rad., Surg.
Eastern Dispensary and Casualty Hospital	Washington, D. C.	Surg.
Freedmen's Hospital ★	Washington, D. C.	Card. Dis., Int. Med., Ob.-Gyn., Ophth., Ortho. Surg., Ped., Psych., Pul. Dis., Rad., Surg., Urol.
Georgetown University Hospital ★	Washington, D. C.	Anes., Int. Med., Neur., Neuro. Surg., Ob.-Gyn., Ophth., Path., Ped., Phys. Med., Psych., Rad., Surg., Urol.
George Washington University Hospital ★	Washington, D. C.	Anes., Card. Dis., Int. Med., Neur., Neuro. Surg., Ob.-Gyn., Path., Phys. Med., Plas. Surg., Psych., Pul. Dis., Rad., Surg , Thor. Surg.
Providence Hospital ★	Washington, D. C.	Anes., Int. Med., Ob.-Gyn., Path., Surg.
St. Elizabeth's Hospital ★	Washington, D. C.	Psych.
Sibley Memorial Hospital ★	Washington, D. C.	Ob.-Gyn., Path., Surg.
Tuberculosis Sanatorium (Glenn Dale, Md.)	Washington, D. C.	Pul. Dis.
Veterans Admin. Hospital	Washington, D. C.	Int. Med., Neur., Ophth., Path., Rad., Surg., Urol.
Washington Hospital Center ★	Washington, D. C.	Anes., Int. Med., Ob.-Gyn., Ophth., Ortho. Surg., Otol , Path., Rad., Surg.
Veterans Admin. Hospital	Coral Gables, Fla.	Int. Med., Path., Phys. Med., Surg.
Halifax District Hospital	Daytona Beach, Fla.	Gen'l Pract.
Broward General Hospital	Fort Lauderdale, Fla.	Path.
University of Florida Teaching Hospital and Clinics	Gainesville, Fla.	Int. Med., Psych.
Baptist Memorial Hospital ★	Jacksonville, Fla.	Gen'l Pract., Path.
Duval Medical Center ★	Jacksonville, Fla.	Int. Med., Ob.-Gyn., Path., Ped., Psych., Surg , Urol.
Hope Haven Hospital	Jacksonville, Fla.	Ortho. Surg.
Riverside Hospital	Jacksonville, Fla.	Int. Med., Surg.
St. Luke's Hospital ★	Jacksonville, Fla.	Gen'l Pract., Int. Med., Ob.-Gyn., Surg.
St. Vincent's Hospital ★	Jacksonville, Fla.	Gen'l Pract., Int. Med., Ob.-Gyn., Path., Ped., Surg., Urol.
State of Florida	Jacksonville, Fla.	Pub. Health
Southeast Florida Tuberculosis Hospital	Lantana, Fla.	Pul. Dis.
Jackson Memorial Hospital ★	Miami, Fla.	Anes., Card. Dis., Derm., Int. Med., Neur., Ob.-Gyn., Ophth., Ortho. Surg., Otol., Path., Ped., Psych., Pul. Dis., Rad. Surg., Urol.
Variety Children's Hospital	Miami, Fla.	Ortho. Surg., Ped.
Mount Sinai Hospital of Greater Miami ★	Miami Beach, Fla.	Int. Med., Ob.-Gyn., Path., Surg.
St. Francis Hospital ★	Miami Beach, Fla.	Int. Med., Ob.-Gyn., Surg.
Orange Memorial Hospital ★	Orlando, Fla.	Int. Med., Ob.-Gyn., Ortho. Surg., Path., Surg., Urol.
Baptist Hospital	Pensacola, Fla	Gen'l Pract., Path.
Sacred Heart Hospital ★	Pensacola, Fla.	Gen'l Pract.
U. S. Navy School of Aviation Medicine	Pensacola, Fla.	Aviat. Med.
American Legion Hospital for Crippled Children	St. Petersburg, Fla.	Ortho. Surg.
Mound Park Hospital ★	St. Petersburg, Fla.	Gen'l Pract., Ob.-Gyn., Surg.
Southwest Florida Tuberculosis Hospital	Tampa, Fla.	Pul. Dis.
Tampa General Hospital ★	Tampa, Fla.	Int. Med., Ob.-Gyn., Ortho. Surg., Otol., Surg.
Crawford W. Long Memorial Hospital ★	Atlanta, Ga.	Int. Med., Ob.-Gyn., Path., Ped., Rad., Surg.
Georgia Baptist Hospital ★	Atlanta, Ga.	Int. Med., Ob.-Gyn., Ortho. Surg., Path., Ped., Surg.
Grady Memorial Hospital ★	Atlanta, Ga.	Int. Med., Neuro. Surg., Ob.-Gyn., Ophth., Ortho. Surg., Path., Ped., Rad., Surg , Thor. Surg., Urol.
Henrietta Egleston Hospital for Children	Atlanta, Ga.	Ped.
Piedmont Hospital ★	Atlanta, Ga.	Int. Med., Ob.-Gyn., Rad., Surg.
St. Joseph's Infirmary ★	Atlanta, Ga.	Card. Dis., Int. Med., Ob.-Gyn., Path., Ped., Surg., Urol.
State of Georgia	Atlanta, Ga.	Pub. Health
Veterans Admin. Hospital ★	Atlanta, Ga.	Int. Med., Ophth., Path., Rad., Surg., Urol.
Eugene Talmadge Memorial Hospital ★	Augusta, Ga	Anes., Int. Med., Neuro. Surg., Ob.-Gyn., Ophth., Ortho. Surg., Path., Ped., Psych., Rad., Surg., Thor. Surg., Urol.

★ Indicates hospitals approved for training interns.

APPROVED RESIDENCY TRAINING PROGRAMS

Name	Location	Approved Residencies
University Hospital ★	Augusta, Ga.	Anes., Int. Med., Neuro. Surg., Ob.-Gyn., Ortho. Surg., Path., Ped., Psych., Rad., Surg., Urol.
Veterans Admin. Hospital	Augusta, Ga.	Int. Med., Neuro. Surg., Psych., Rad., Surg.
The Medical Center ★	Columbus, Ga.	Gen'l Pract.
Scottish Rite Hospital for Crippled Children	Decatur, Ga.	Ortho. Surg.
Emory University Hospital ★	Emory University, Ga.	Anes., Card. Dis., Int. Med., Neuro. Surg., Ortho. Surg., Path., Phys. Med., Rad., Surg., Thor. Surg.
U. S. Army Hospital ★	Fort Benning, Ga.	Surg.
John L. Hutcheson Memorial Tri-County Hospital	Fort Oglethorpe, Ga.	Gen'l Pract.
Macon Hospital ★	Macon, Ga.	Gen'l Pract., Ob.-Gyn., Surg.
Memorial Hospital of Chatham County ★	Savannah, Ga.	Anes., Int. Med., Ob.-Gyn., Path., Surg., Urol.
Georgia Warm Springs Foundation	Warm Springs, Ga.	Phys. Med.
Kapiolani Maternity and Gynecological Hospital	Honolulu, Hawaii	Ob.-Gyn.
Kauikeolani Children's Hospital	Honolulu, Hawaii	Ped.
Leahi Hospital	Honolulu, Hawaii	Pul. Dis., Thor. Surg.
Queen's Hospital ★	Honolulu, Hawaii	Int. Med., Ob.-Gyn., Path., Psych., Surg.
St. Francis Hospital ★	Honolulu, Hawaii	Int. Med., Ob.-Gyn., Path.
Shriners Hospitals for Crippled Children	Honolulu, Hawaii	Ortho. Surg.
Tripler Army Hospital ★	Honolulu, Hawaii	Int. Med., Ob.-Gyn., Ortho. Surg., Path., Ped., Rad., Surg., Urol.
Territorial Hospital	Kaneohe, Hawaii	Psych
MacNeal Memorial Hospital ★	Berwyn, Ill	Gen'l Pract., Surg.
Alexian Brothers Hospital	Chicago	Path., Surg.
American Hospital ★	Chicago	Path., Surg.
Augustana Hospital ★	Chicago	Int. Med., Obst., Path., Rad., Surg.
Chicago Eye, Ear, Nose and Throat College and Hospital	Chicago	Ophth.
Chicago Maternity Center	Chicago	Obst.
Chicago State Hospital	Chicago	Psych.
Chicago State Tuberculosis Sanitarium	Chicago	Pul. Dis., Thor. Surg
Chicago Wesley Memorial Hospital ★	Chicago	Anes., Int. Med., Neur., Neuro. Surg., Ob.-Gyn., Ophth., Ortho. Surg., Otol., Path., Psych., Rad., Surg., Urol.

★ Indicates hospitals approved for training interns.

GOVERNMENT SERVICES

VETERANS ADMINISTRATION

New Atomic Reactor.—An atomic reactor, believed to be the largest ever installed in a hospital and one of the first designed specifically for medical purposes, was placed in operation at the Veterans Administration hospital in Omaha. It is housed in a vertical concrete tube 22 ft. deep and 6.5 ft. in diameter, sunk into the ground beneath the hospital. Nestled in this, it floats in 4,750 gallons of triple-distilled water which acts as a shield against escape of radioactivity. A built-in safety device eliminates any danger of an atomic explosion. The fuel rods are of a material that stops the nuclear reaction when excessive heat is generated.

It is expected that the generator will simplify performance of many tests on the blood, liver, muscle, and other tissues formerly performed by tedious and time-consuming chemical methods. The specimen to be analyzed is placed in the reactor, where it becomes radioactive. The radiation from it then is detected by a 100-channel energy-level analyzer, which produces a graph indicating the chemical makeup. It has been found, for example, that the blood level of zinc decreases markedly immediately after a heart attack. The electrocardiogram does not always differentiate at an early stage between heart attack and some other condition, such as a gastrointestinal upset, but the reactor should accomplish this. By producing radioisotopes, it will enable the Veterans Administration to increase its use of these substances for treatment and research.

Veterans Administration hospitals will still use radioisotopes supplied by the Atomic Energy Commission, but there are a number of radioisotopes that have effective lives too short to allow time for shipment from the usual sources. Some of these, such as chlorine-38, bromine-82, sodium-24, potassium-42, and copper-64, will be widely used in diagnosis and therapy. In addition to its safety design, the new reactor has these advantages: 1. It will operate at temperatures low enough so that live mice may be placed in it. This would be impossible in most other reactors. 2. It will use uranium at a rate so slow that the core material will last almost indefinitely. 3. It is so designed that samples can be run in and out quickly.

PUBLIC HEALTH SERVICE

Training in Epidemiology.—A multidisciplinary course in principles of epidemiology will be offered at the Communicable Disease Center, Public Health Service, Atlanta, Ga., Jan. 11-15, 1960, as a part of the continuing program of the Center's training branch. Designed to provide public health workers with a basic understanding of how epidemiologic techniques can be used in an approach to the solution of problems in the preventable disease field, the course is offered for the following categories of public health personnel: physicians, dentists, veterinarians, nurses, laboratory workers, environmental health personnel, and other members of the public health term. Participants will be selected on the basis of professional education and experience and current responsibility in public health programs at all levels of government. Preference will be given to persons whose professional tasks involve the application of epidemiologic procedures, and registrants will be expected to attend all sessions of the course. Further information and application forms may be obtained from the chief of the Communicable Disease Center, Public Health Service, 50 Seventh St., N. E., Atlanta 23, Ga., to the attention of the chief of the training branch.

MEDICAL NEWS

CALIFORNA

Hospital Conference on Hallucinogenic Drug.—The first invitational conference of Napa State Hospital, Imola, a symposium on lysergic acid diethylamide (LSD-25), will be presented for staff and guests on Saturday, Jan. 16, sponsored jointly by the hospital and Sandoz Pharmaceuticals. Basic science aspects of this hallucinogenic drug will be discussed during the morning, and the afternoon session will encompass the clinical and therapeutic status of the drug. Dr. Sidney V. Cohen, chairman, research committee, Veterans Administration Center, Neuropsychiatric Hospital, Los Angeles, will be the guest lecturer. Other participants will include faculty members from Stanford and the University of California Medical School, Langley Porter Neuropsychiatric Institute, and practicing psychiatrists and psychologists.

CONNECTICUT

British Epidemiologist Named Public Health Chairman.—Dr. Anthony Monck-Mason Payne, of Great Britain, who is now chief medical officer for endemo-epidemic diseases of the World Health Organization in Geneva, will become Anna M. R. Lauder Professor of Public Health and chairman of a reorganized department of epidemiology and public health at Yale University, New Haven, July 1. He succeeds Prof. Ira V. Hiscock, who is retiring after serving on the Yale faculty since 1920. The new appointment marks a major reorganization within the Yale School of Medicine whereby the public health department and the section of epidemiology and preventive medicine will be combined under Dr. Payne with the collaboration of Dr. John R. Paul. The program of graduate training for students entering a variety of public health activities and leading to the master of public health degree will be continued, but opportunity for advanced study in epidemiology in its broadest sense will be emphasized.

FLORIDA

Annual Cardiovascular Seminar.—The second annual Hillsborough County and Suncoast Cardiovascular Seminar will be held Saturday and Sunday, Feb. 20-21, at the Hillsboro Hotel, Tampa. Programs will be presented from 9 a. m. until 4 p. m. each day. This seminar is jointly sponsored by the Hillsborough County Heart Association, Tampa, and the Suncoat Heart Association, St. Petersburg. Six specialists in diagnosis, treatment, and surgery in the cardiovascular field will present lectures and take part in panel discussions, which will be held at lunch both days and at the close of each day's program. Participants include Dr. Samuel A. Levine, Boston; Dr. Samuel Kaplan, Cincinnati; Dr. Robert Bruce Logue, Atlanta, Ga.; Dr. Richard G. Lester, Minneapolis; Dr. C. Walton Lillehei, Minneapolis; and Dr. Lawrence E. Lamb, School of Aviation Medicine, Brook Air Base, Texas. All physicians are invited. No registration fee will be charged.

ILLINOIS

Fellowship in Allergy.—Northwestern University Medical School offers a fellowship in allergy beginning about July 1, 1960 (or earlier). The following types of candidates will be considered: those who have had two years of residency in internal medicine or pediatrics; those who have completed their formal training requirements for these certifying boards; those who have completed their formal allergy training or experience and desire a period with special emphasis on investigative problems. The annual stipend is $3,600-$5,000, depending on family status and educational background. Address inquiries to Dr. Samuel M. Feinberg, Northwestern University Medical School, 303 E. Chicago Ave., Chicago 11.

Chicago

Meeting of Ileoptimists.—Dr. Joseph B. Kirsner, professor of medicine, University of Chicago, will speak to the Ileoptimists Inc., of Chicago on Monday, Dec. 28, at 222 W. Adams St. at 7:30 p. m. His talk, "The Nature of Ulcerative Colitis," will be accompanied by colored slides. The purpose of the Ileoptimists is to help individuals in the proper care of and adjustment to ileostomies. For information, contact the president, Mr. Matt Martel at 27 S. Elm, Northlake, Ill. Mr. Martel's telephone number is FIllmore 3-9041.

Report Following Hospital Merger.—The Presbyterian-St. Luke's Hospital released a report on its record of accomplishments following the merger of the two hospitals. Last year the hospital provided 269,800 days of hospital care for 25,300 in-patients. Out-patients made 90,000 clinic visits. The hospital, which recently completed its main building has its

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

medical science research building under construction to supply new and expanded laboratory and surgical services. Presbyterian–St. Luke's is a voluntary nonprofit hospital and an affiliated teaching unit of the College of Medicine of the University of Illinois. A private hospital, it is dependent for its support on the people of Chicago and the midwest.

Dr. Katz Gives Annual Lecture.—Dr. Louis N. Katz was presented the third honorary lectureship award of Albany Medical College of Union University Nov. 19. Prior to the award, Dr. Katz gave a lecture, "Energy of the Beating Heart." The award cerenies were initiated by Harold C. Wiggers, Ph.D., n of Albany Medical College, and son of Dr. arl J. Wiggers, under whom Dr. Katz studied at Western Reserve University School of Medicine, Cleveland. Since 1930, Dr. Katz has been director of the cardiovascular research department at the Medical Research Institute of the Michael Reese Hospital in Chicago. The honorary lectureship, which recognizes "distinguished service to mankind in the fields of science, medicine and teaching," is Albany Medical College's highest honor.

Lectures on Growth of Medicine.—Northwestern University Medical School announced the sixth annual series of lectures on "The Growth of Medicine." The one-hour talks will be given every Tuesday at 8 a. m. in room 641 of the Medical School, 303 E. Chicago Ave., Chicago. The series has been planned under the chairmanship of Dr. Frederick W. Stenn, assistant professor of medicine. Members of the medical profession and the public are invited. The lectures and lecturers are as follows:

Jan. 5.—The Evolution of Quackery, Dr. Morris Fishbein, professor emeritus of medicine, University of Illinois College of Medicine.
Jan. 12.—The History of Faith Healing, Rev. Richard Dahl, chaplain, Chicago Wesley Memorial Hospital.
Jan. 19.—Dawn of Histology, Leslie B. Arey, Ph.D., professor of anatomy emeritus, Northwestern University Medical School.
Jan. 26.—Emergence of Modern Medicine from Ancient Folkways, Dr. Walter C. Alvarez, professor of medicine, emeritus, University of Minnesota Mayo Foundation.
Feb. 2.—They Were Also Patients: George Gershwin, Clarence Darrow and Adolph Hiter, Dr. Noah D. Fabricant, associate editor, *Ear, Eye, Nose & Throat Monthly.*
Feb. 9.—The Medical Revolution, Dr. Lester S. King, clinical professor of pathology, University of Illinois College of Medicine.
Feb. 16.—The History of Vascular Surgery, Dr. William S. Dye Jr., clinical associate professor of surgery, University of Illinois College of Medicine.
Feb. 23.—Medical Illustrations, Mr. Thomas Jones, professor of medical and dental illustrations emeritus, University of Illinois College of Medicine.
March 1.—The Chamberlens and the Obstetric Forceps, Dr. William B. Serbin, assistant professor of obstetrics and gynecology, Northwestern University Medical School.
March 8.—Chest Pain, Its Appreciation Through the Ages, Dr. William H. Wehrmacher, instructor in medicine, Northwestern University Medical School.

KANSAS

Dr. Carter Named Pathology Chairman.—Dr. John R. Carter, from the University of Iowa, Iowa City, was appointed professor of pathology and chairman of the department at the University of Kansas School of Medicine, Kansas City. Dr. Carter, whose appointment is effective Jan. 1, fills the post held for over 10 years by Dr. Robert E. Stowell, who is now scientific director of the Armed Forces Institute of Pathology in Washington, D. C. Dr. Carter has held academic appointments at the University of Iowa, from instructor to professor, since 1944. From 1946 to 1948 he served as assistant and chief pathologist at the Naval Medical School in Bethesda, Md. In April, he was elected to the council of the International Academy of Pathology.

MARYLAND

Veterinarian Receives Animal Care Award.—The Charles A. Giffin Award for 1959 was presented at the 10th annual meeting of the Animal Care Panel to Robert D. Henthorne, D.V.M., chief of the Animal Laboratory Division of Microbiological Associates, Inc., of Bethesda, "in recognition of his work in promoting and developing high standards for the production and use of disease-free animals." The Giffin Award, established in 1956 to honor the late Charles A. Giffin, Veterinary Bacteriologist at the New York State Department of Health Laboratories in Albany, is presented annually "to the person who most significantly advances the concepts of improved laboratory animal quality."

MICHIGAN

Program for Medical Care Research.—A new training program titled "Research in Medical Care" is being offered to graduate students by the University of Michigan's School of Public Health. The program, supported by a five-year grant from the Ford Foundation, is designed chiefly to train graduates in the effect of social factors on the health care of the aged. A limited number of paid research assistantships are available to students with a background in public health, social work, economics, sociology, and certain other social sciences. To be eligible, the student must be accepted into a graduate program at the U-M in one of these fields. Training includes an introduction to medical care, study of the social factors in health organization, and the preparation and carrying out of research projects. Dr. Solomon J. Axelrod, director of the U-M Bureau of Public Health Economics, is in charge of the program. The first applications will be due Feb. 1 from students wishing to enter the program next fall.

NEW YORK

Hospital Program for Visiting Professors.—Beginning next July 1 with the start of the new academic year, Highland Hospital, Rochester, will institute a new program of visiting professorships designed to intensify graduate training for medical interns and residents and to provide educational "refresher" facilities for the 300 doctors who are on the attending staff. The program, announced by Dr. Jacob W. Holler, chief of medicine and director of graduate education, calls for the teaching services of at least six "outstanding" medical professors drawn from the faculties of medical institutions in the United States and Canada, who will be medical specialists in medicine, surgery, obstetrics and gynecology, pediatrics, and various subspecialties.

Society News.—The officers of the New York Allergy Society are as follows: president, Dr. S. Senior Sack, Flushing; president-elect, Dr. Joseph H. Fries, Brooklyn; vice-president, Dr. Sheppard Siegal, New York City; secretary, Dr. Ely Perlman, New York City; treasurer, Dr. Murray Dworetzky, New York City, and assistant secretary-treasurer, Dr. Walter R. Kessler, New York City.——On May 11, the New York Academy of Gastroenterology elected officers for 1959-1960: Dr. Michael Weingarten, president; Dr. Joseph R. Van Dyne, president-elect; Dr. Hyman M. Robinson, first vice-president; Dr. Henry Colcher, second vice-president; Dr. Edward J. Nightingale, secretary; Dr. Jerome Weiss, recording secretary; and Dr. William C. Jacobson, treasurer.

New President of Physicians' Home Fund.—Dr. David J. Kaliski, of New York City, was elected president of the Physicians' Home, succeeding Dr. Charles Gordon Heyd, also of New York City, on the 40th anniversary of the home. Dr. Kaliski also becomes the presiding officer of the board of directors and chairman of the home's executive committee. The Physicians' Home is a fund for the maintenance of elderly indigent physicians and surgeons who have been members of the State Medical Society, and doctors' widows and orphans who are eligible. The home maintains offices at the society's headquarters at 750 Third Ave., New York 17. The fund enables beneficiaries to reside wherever they wish, and payments are usually on a permanent basis.

New York City

Library Dedicated.—The Eugene F. Dubois Library was dedicated Nov. 24 by the staff of the Second (Cornell) Medical Division, Bellevue Hospital. Honoring the late physician and physiologist, it occupies the exact site of his pioneer research in human metabolism, begun at Bellevue in 1911.

Foreign Lecturer.—Dr. Francis E. Camps, forensic pathologist of the coroner's office and lecturer in forensic medicine in the London Hospital Medical College, London, England, delivered a lecture entitled "Burden of Proof" at the New York University-Bellevue Medical Center, Nov. 30.

NORTH CAROLINA

Dr. Wells Named Library Regent.—President Dwight D. Eisenhower appointed Dr. Warner L. Wells, associate professor, department of surgery, University of North Carolina School of Medicine, Chapel Hill, as regent of the National Library of Medicine. The library began during the last century as the Army Medical Library. It later became known as the Library of the Surgeon General's Office and later the Armed Forces Medical Library. Last year the name was changed to the National Library of Medicine. It is now a unit of the United States Public Health Service.

Medical Foundation Elects Layman President.—Mr. Paul W. Schenck Jr., Greenboro businessman, was elected president of the Medical Foundation of North Carolina. Mr. Schenck succeeds Dr. Paul F. Whitaker, Kinston, who has held the post since 1956. The purpose of the foundation is to aid and promote medical education, services, and research by giving financial assistance to the University of North Carolina School of Medicine, the UNC School of Nursing, and North Carolina Memorial Hospital. The Medical Foundation of North Carolina was founded in 1949, with Major L. P. McLendon, of Greensboro, as president. It serves as a depository for private funds which are used to forward a good-health program for the entire state.

PENNSYLVANIA

Plan Center for Disturbed Children.—The Eastern Pennsylvania State School and Hospital designed for a rural site in Bensalem Township, Bucks County, will be Pennsylvania's first state institution expressly for the care and treatment of emotionally disturbed children. It will be operated by the Department of Public Welfare and will offer both residential and out-patient care for children with psychiatric disorders referred by custodial and social agencies. The program for the institution calls for a self-contained community, with residential "neighborhoods," a school, recreation-community center, and hospital. Construction will be in two phases. The first phase, valued at about 8 million dollars will have a capacity of 340 patients, and will include a 164-bed clinic building; separate units for food service, recreation, and education, and 12 cottages housing a total of 176 patients. Later, cottages will be built for 148 patients, classroom and recreation space will be expanded, and a 20-bed research unit will be added. New structures for administration, worship, and maintenance are also included in this later phase. Construction is expected to begin in the spring of 1960.

Philadelphia

Building for Laboratory Animals.—Mr. William Goldman, Philadelphia philanthropist, officiated at the opening of a large, newly reconstructed animal colony for medical research donated by him to

Hahnemann Medical College. The three-story building facing Vine Street within the Hahnemann "block" will house laboratory animals in use in Hahnemann's research program. The $1,000,000 research program at 112-year-old Hahnemann covers more than 97 projects centered mainly in heart disease and cancer. The gift by Mr. Goldman to Hahnemann College is the latest of a number of sizable benefactions to the institution by the philanthropist, including the William Goldman Radio-Isotope Laboratory.

Annual Lecture.—The annual Phi Delta Epsilon Lectureship under the auspices of the Sigma Chapter at the Temple University School of Medicine, will be held Feb. 17. The lecturer will be Dr. Seymour S. Kety, chief, National Institute of Mental Health, Bethesda, Md., who will speak on the biologic aspects of schizophrenia.

Personal.—Dr. Harry E. Bacon who served as honorary professor at the University of Guayaquil was awarded the "Oficer de Order Al Merito" by the Republic of Ecuador, recently.——Marion Fay, Ph.D., president and dean of Woman's Medical College of Pennsylvania, was elected an honorary fellow in the College of Physicians of Philadelphia on Oct. 7.

Hospital Receives Research Grant.—The eighth grant made since 1954 to Pennsylvania Hospital by the John A. Hartford Foundation, Inc., of New York City, was announced Dec. 6. The latest award of $351,120, which brings to $1,320,000 the amount given by the foundation to the hospital for scientific research and special programs, will be used over a three-year period to study diseases of the gastrointestinal tract and the relationship of endocrine glands and stress on peptic ulcer formation. The Hartford Foundation was originally established by John A. Hartford to distribute his personal charitable donations. His brother George L. Hartford, who died in 1957, left his entire estate to the foundation. John A. Hartford was president of the Great Atlantic & Pacific Tea Company and George L. Hartford was chairman of the board.

TEXAS

New Dallas Hospital Dedicated.—Dedication ceremonies of the $4,500,000 Women and Children's Hospital, newest addition to the facilities of the Baylor University Medical Center in Dallas, were held Oct. 22. The first new patients were admitted to the hospital on Oct. 28. All maternity patients and children in Baylor's Pediatric Division in the former Maternity Division of Baylor were moved into the new Women and Children's Hospital. The new hospital contains 196,000 square feet and two wings of seven stories each, plus a full basement and two-story machinery penthouse. A bedside service panel developed at Baylor will permit the patient to control television, select from five radio channels, piped in music, or chapel services. The medical center now is composed of three hospitals: George W. Truett Medical and Surgical Hospital, Women and Children's Hospital, and the Minnie S. Veal Teaching and Research Hospital. Originally the hospital was named the Texas Baptist Memorial Sanitarium. In 1920, the name became the Baylor Hospital; in 1936, the name was changed to the Baylor University Hospital.

GENERAL

Obstetricians and Gynecologists Change Office.—The American College of Obstetricians and Gynecologists announced that as of Sept. 20 its administrative office is located at 79 W. Monroe St., Room 1120, Chicago 3. The telephone number will remain FRanklin 2-3124.

Bacteriologists to Meet in Philadelphia.—The 60th annual meeting of the Society of American Bacteriologists, will be held in Philadelphia. The meeting, to be held May 1-5, will feature more than 450 papers dealing with "latest research findings in bacteriology and microbiology," said Harry E. Morton, Ph.D., meeting chairman. Dr. Morton, professor of bacteriology at the School of Medicine of the University of Pennsylvania, said that a minimum of seven sessions would be held simultaneously in three mid-Philadelphia hotels.

Bahamas Allergy Conference.—The first Bahamas Allergy Conference will take place at the Nassau Beach Lodge, Nassau, Bahamas, March 5-12, 1960. About 40 speakers will talk on various phases of allergy and there will be time for discussion. The meeting will follow the 16th annual congress of the American College of Allergists, which will be held at the Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-March 4. For information, write Dr. Leon Unger, 185 N. Wabash Ave., Chicago 1.

Mr. E. R. Loveland Retires.—Mr. Edward R. Loveland, F. A. C. P. (Hon.) will retire Dec. 31 as executive secretary of the American College of Physicians after completing nearly 34 years of service to the college. He became the executive secretary on April 4, 1926, and without delay undertook the establishment of the college headquarters in Philadelphia and the development of an efficient administrative program. Mr. Loveland will be succeeded by Dr. Edward C. Rosenow Jr., executive director of the Los Angeles County Medical Association, who will take office on Jan. 1. Dr. Rosenow received his M.D. degree from Harvard Medical School, Boston, and M.S. (Med.) degree from the University of Minnesota, Mayo Foundation, Rochester, Minn.

Heart Chairmen Named.—Mrs. Dwight D. Eisenhower and Dr. Paul Dudley White will serve as honorary chairman and co-chairman, respectively, of the 1960 national Heart Fund drive. This will mark their third successive year as campaign aides in these capacities. The 1960 Heart Fund drive, to be conducted throughout the nation by the American Heart Association and its affiliates during the month of February, is based on the slogan "Heart Disease—Number One Enemy, Heart Fund—Number One Defense."

Report on Traffic Fatalities.—The nation's traffic death toll came down in October for the first time in 1959, the National Safety Council reported Dec. 4. The October toll, 3,420 highway fatalities, not only was 5% below the same month last year (3,600) but was the lowest for any October since 1949. The death toll for the first 10 months of this year was 2% above the same period last year—as contrasted with a 5% increase at the end of the first seven months and with monthly increases earlier in the year that ranged up to 8%. The 10-month toll was 30,560, as compared with 29,870 for the same period in 1958. Disabling injuries from traffic accidents in the 10-month period were estimated at 1.1 million.

Psychosomatic Meeting in Montreal.—The American Psychosomatic Society's 17th annual meeting will be held at the Sheraton-Mt. Royal Hotel, Montreal, on Saturday and Sunday, March 26 and 27. The program will consist of four sessions, three of which will be general. A half-day special session, on Sunday morning, will be allotted to the panel presentation, "Contributions of Behavioral Scientists to Psychosomatic Medicine." Panel speakers will represent fields of anthropology, medicine, psychiatry, and sociology. The registration fee for nonmembers is $5. Students, interns, residents, and fellows will be admitted to the sessions upon payment of $1. The society will hold its annual cooperative cocktail party following the Saturday afternoon session. For information, write the American Psychosomatic Society, 265 Nassau Road, Roosevelt, N. Y.

Proctology Award Contest.—The International Academy of Proctology announced its annual cash prize and certificate of merit award contest for 1959-1960. The best unpublished contribution on proctology or allied subjects will be awarded $100 and a certificate of merit. The winning contribution will be selected by a board of judges, and all decisions are final. The formal award of the first prize, and presentation of other certificates, will be made at the annual convention dinner dance of the International Academy of Proctology, April 27, 1960, at the Americana Hotel, Miami Beach, Fla. The academy reserves the exclusive right to publish all contributions in its official publication, *The American Journal of Proctology*. All entries are limited to 5,000 words, must be typewritten in English, and submitted in five copies. Entries must be received no later than Feb. 1. Entries should be addressed to Dr. Alfred J. Cantor, Executive Officer, International Academy of Proctology, 147-41 Sanford Ave., Flushing 55, N. Y.

Meeting of Orthopedists.—The 27th annual meeting of the American Academy of Orthopaedic Surgeons, Inc., will be held Jan. 23-28 at the Palmer House, Chicago. The presidential address will be given by Dr. Harold A. Sofield, Oak Park, Ill., the morning of Jan. 25. Papers to be presented by special invitation include "The Fracture of the Carpal Scaphoid," by Prof. Otto Russe, Vienna, Austria, and "Paralytic Scoliosis," by Prof. J. I. P. James, Edinburg, Scotland. An audio-visual program will be conducted each day and will include the following presentations by foreign producers:

Recurrent Dislocation of the Shoulder, Dr. Herbert F. Moseley, Montreal, Quebec, Canada.
Arthroplasty of Elbow and Knee, Prof. Oscar Scaglietti, Florence, Italy.

Instructional courses and scientific exhibits are planned. The annual banquet will be held the evening of Jan. 27. The 28th annual meeting will be held at the Americana Hotel, Bal Harbour, Fla., Jan. 8-13, 1961.

Cancer Conference in Minneapolis.—The fourth International Cancer Conference sponsored by the American Cancer Society and the International Cancer Institute will be held in Minneapolis Sept. 13-15 under the theme, "Changing Concepts Concerning Cancer." Dr. Michael B. Shimkin, Bethesda, Md., will open the meeting with an address on the theme. Panel discussions are planned on cancer etiology, cancer pathogenesis, and cancer therapy. Symposiums are listed as follows:

Cancer of the Breast
Cancer of the Lung
Cancer of the Female Genital Tract
Cancer of the Gastrointestinal Tract
Cancer of the Male Genitourinary Tract
Leukemias and Lymphomas
Cancer of the Skin
Cancer of the Head and Neck
Cancer Control

For information, write the American Cancer Society, Inc., Medical Affairs Department, 521 West 57th St., New York 19.

Brazilian Physician Awarded Rehabilitation Fellowship.—The awarding of a Pfizer Fellowship in Rehabilitation to Dr. Haroldo Campos Guimaraes, or Sao Paulo, Brazil, was announced Nov. 27, in Rio de Janeiro, Brazil, by the Ambassador of the United States to Brazil, Hon. John M. Cabot. The Pfizer Fellowship in Rehabilitation has been created by the World Rehabilitation Fund through funds made available by Chas. Pfizer & Co., Inc. Dr. Howard A. Rusk, New York City, president, World Rehabilitation Fund, participated in the reception at the American Embassy at which Ambassador Cabot made the announcement. Dr. Guimaraes is currently a member of the staff of the Instituto Nacional de Rehabilitacao–Clinica Ortopedica de Traumatologica of the Medical Faculty of the University of Sao Paulo. Dr. Rusk explained that the Pfizer Fellowship was being given by the World Rehabilitation Fund in cooperation with the International Society for the Welfare of Cripples and its affiliate in Brazil, the Associacao de Assistencia a Crianca Defeituosa. He said Dr. Guimaraes' postgraduate training would begin Jan. 1 at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center.

Triological Meeting in Philadelphia.—The American Laryngological, Rhinological, and Otological Society, Inc., the Triological Society, will hold an eastern sectional meeting Jan. 8 at the Warwick Hotel, Philadelphia. Dr. Theodore E. Walsh, St. Louis, president of the society, will open the meeting. The program includes the following papers:

Carcinoma of the Tonsil, Drs. John F. Daly, Milton Friedman, New York City.

The Clinical Characteristics of Vertiginous Epilepsy, Dr. Bernard J. Alpers, Philadelphia.

Problems and Complications in Head and Neck Surgery, Dr. George A. Sisson, Syracuse, N. Y.

Cancer of the Ear (A Review of 150 Surgically Treated Cases), Dr. John S. Lewis, New York City.

Viral Infections of the Respiratory Tract, Dr. Walter Havens Jr., Philadelphia.

Malignancy of the Salivary Glands: A Follow-up Survey, Dr. Frank D. Lathrop, Boston.

Experiences with the Fenestra Ovalis Technique of Shea, Dr. David Myers, S. D. Erukar, Ph.D., Dr. Woodrow D. Schlosser, Dr. Lindsay Pratt, and Richard A. Winchester, Ph.D., Philadelphia.

For information, write Dr. Floyd J. Putney, Vice-President, Triological Society, 712 Locust St., Philadelphia 3.

Society News.—The **American Association for the Surgery of Trauma** officers for 1959-1960 are: president, Dr. James K. Stack, Chicago; president-elect, Dr. Harrison L. McLauchlin, New York City; vice-president, Dr. Preston A. Wade, New York; secretary, Dr. William T. Fitts Jr., Philadelphia; treasurer, Dr. Raymond Householder, Chicago; and recorder, Mr. Fraser N. Gurd, Montreal, Que. The next annual meeting will be held at the Hotel del Coronado, Coronado, Calif., Oct. 5-7.——The elected officers of the **Central Association of Obstetricians and Gynecologists** are: president, Dr. Isadore Dyer, New Orleans; president-elect, Dr. Edwin J. DeCosta, Chicago; vice-president, Dr. Joseph G. Webster, Kansas City, Mo.; secretary-treasurer, Dr. Herman L. Gardner, Houston, Texas; and assistant secretary, Dr. Roy G. Holly, Omaha.——The 1960 officers of the **Mississippi Valley Medical Society** are as follows: president-elect, Dr. Preston C. Hall, St. Louis; vice-president for Illinois, Dr. Lee N. Hamm, Lincoln; vice-president for Iowa, Dr. Paul J. Leehey, Independence; vice-president for Kansas, Dr. Clarence H. Benage, Pittsburg; vice-president for Minnesota, Dr. Bernard C. Glueck Jr., Minneapolis; vice-president for Missouri, Dr. Jack M. Martt, Columbia; vice-president for Nebraska, Dr. Clyde L. Kleager, Hastings; vice-president for North Dakota, Dr. Reuben H. Waldschmidt, Bismarck; vice-president for South Dakota, Dr. Alonzo P. Peeke, Volga; vice-president for Wisconsin, Dr. Wallace Marshall, Watertown; and accounting officer, Dr. Harold Swanberg, Quincy, Ill.

LATIN AMERICA

Ophthalmologists Transfer Meeting Site.—The sixth Pan American Congress of Ophthalmology, scheduled to meet in Caracas, Venezuela, Jan. 31 to Feb. 6, has been transferred to the Club Puerto Azul, on the ocean about an hour's drive from Caracas, Dr. Brittain F. Payne, New York City, president of the Pan American Association of Ophthalmology, announced Dec. 4. Physicians may make reservations through Mr. Thomas D. Callahan, Manager, World Wide Travel Department, AAA, LaSalle at 13th Street, Minneapolis 3, Minn.

Radiology Congress in Mexico.—The first National Congress of Radiology and third Mexican Radiologic Technical Exhibit will be held on Feb. 7-13 in the University City of Mexico City. Dr. Jose Alvarez Amezquita, the Ministry of Public Health and Social Assistance, will be the honorary president. The program includes lectures, symposiums, and presentation of films, and round-table discussions. On Feb. 11, a session of the executive committee will be held at 5 p. m. For information, write Sociedad Mexicana de Radiologia, Calle de Coahuila 35, Mexico 7, D. F., Mexico.

FOREIGN

Change Dates for Film Prize.—The annual Prize of the Medico-Surgical Cinema of "Presse Médicale" will be awarded March 22, 1960, at the new Faculty of Medicine instead of April 5 as it had been previously published. Candidatures and films must be directed to the Secretary's office of the Journal, la Presse Médicale, 120, Boulevard Saint-Germain, Paris VI, before Feb. 15.

Teaching Film Program.—The German Medical Association, host of the 14th general assembly of the World Medical Association, scheduled to convene in West Berlin, Sept. 15-21, is planning to have an extensive medical film program. All medical associations are cordially invited to present to the German Medical Association their recommendations as to outstanding postgraduate medical teaching films particularly those produced in their country, which should be given consideration by the special committee appointed to select the films to be shown. The World Medical Association Headquarters Secretariat, 10 Columbus Circle, New York 19, is issuing a special "Film Recommendation Sheet" for the use of the member associations.

CORRECTION

Therapy for Lipid Pneumonia.—In The Journal, Nov. 28, page 1810, in the article by Dr. Joshua Seidel, entitled "Mucolytic Aerosol Therapy for Lipid Pneumonia," an error appears. Line 10 of the second column on page 1812, which reads, "although the lesions had cleared by x-ray therapy," should read, "although roentgenographic studies showed clearing of the lesions."

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II, Various Cities, April 19-20. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 21-23. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Connecticut:* *Regular. Examination.* Hartford, Mar. 8-10. Sec., Dr. Stanley B. Weld, 160 St. Ronan St., New Haven. *Homeopathic. Examination.* Derby, Mar. 8. Sec., Dr. Ronald A. Davis, 38 Elizabeth St., Dover.

Delaware: *Examination.* Dover, Jan. 12-14. *Endorsement.* Dover, Jan. 21. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Georgia: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Examination.* Honolulu, Jan. 11-12. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination* and *Reciprocity.* Boise, Jan. 11, 12, 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Indiana: *Examination.* Indianapolis, June 1960. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Kansas:* *Examination and Reciprocity.* Kansas City, Jan. 15-16. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Massachusetts: *Examination.* Boston, Jan. 12-15. Sec., Dr. David W. Wallwork, Room 37, State House, Boston.

Minnesota:* *Examination.* Minneapolis, Jan. 19-21. *Reciprocity.* Minneapolis, Jan. 21. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

Mississippi: *Examination.* Jackson, June. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

Montana: *Examination and Reciprocity.* Helena, April 5. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

New Hampshire: *Examination.* Concord, March 9-11. *Reciprocity.* Concord, March 9. Sec., Dr. Edward W. Colby, 61 South State St., Concord.

New Jersey: *Examination.* Jan. 19-22. *Reciprocity.* Monthly, Admin. Sec., Michael E. H. Sweeney, 28 West State St., Trenton.

North Carolina: *Reciprocity.* Southern Pines, Jan. 8. Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

North Dakota: *Examination.* Grand Forks, Jan. 6-8. *Reciprocity.* Grand Forks, Jan. 9. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

Oklahoma:* *Examination.* Oklahoma City, May 31-June 1. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Oregon:* *Examination.* Portland, Jan. 12-13. *Reciprocity.* Portland, Jan. 14-16. Ex. Sec., Mr. Howard J. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination.* Philadelphia, January. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

Rhode Island:* *Examination.* Providence, Jan. 7-8. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Dakota:* *Examination.* Sioux Falls, Jan. 19-20. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Utah: *Examination.* Salt Lake City, July 6-8. Director, Mr. Frank E. Lees, 324 State Office Bldg., Salt Lake City 1.

Washington:* *Examination.* Seattle, Jan. 11-13. Administrator, Professional Division, Capitol Bldg., Olympia.

West Virginia: *Examination.* Charleston, Jan. 11-13. Sec., Dr. Newman H. Dyer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:* *Examination.* Madison, Jan. 14-16. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Building, 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, Feb. 1. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arkansas: *Examination.* Little Rock, April 21-22. Sec., Dr. A. W. Ford, Department of Education, Education Bldg., Little Rock.

Colorado: *Examination and Reciprocity.* Denver, March 2-3. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination.* New Haven, Feb. 13. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

Iowa: *Examination.* Des Moines, Jan. 12. *Reciprocity.* Des Moines, Jan. 11. Sec., Dr. Elmer W. Hertel, Waverly.

Kansas: *Examination.* Kansas City, June 10-12. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburg.

Michigan: *Examination.* Detroit and Ann Arbor, Feb. 12-13. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

Minnesota: *Examination.* Minneapolis, Jan. 5-6. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14.

New Mexico: *Examination.* Santa Fe, Jan. 17. *Reciprocity.* Santa Fe, Jan. 9. Sec., Mrs. Marguerite Cantrell, Box 1522, Santa Fe.

Oklahoma: *Examination.* Oklahoma City, April 15-16. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Texas: *Examination.* Austin, Houston, Galveston and possibly Dallas, April 15-16. Sec., Dr. Cornelia M. Smith, State Office Bldg., 201 East 14th St., Austin.

Washington: *Examination.* Seattle, Jan. 6-7. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

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*Basic Science Certificate required.

DEATHS

Alexander, John Gordon Ⓜ Glen Burnie, Md.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1910; veteran of World War I; staff member, Maryland General Hospital in Baltimore; died Sept. 16, aged 68.

Barnes, Finis E., Charleston, Ill.; American Medical College, St. Louis, 1903; died Sept. 30, aged 86.

Beyer, Arthur Ray Ⓜ Tampa, Fla.; Louisville (Ky.) Medical College, 1907; member of the Southeastern Surgical Congress and the Aero Medical Association; fellow of the International College of Surgeons; past-president of the Seaboard Airline Railway Surgeons Association; died Sept. 27, aged 79.

Carswell, Robert Lee Ⓜ Colonel, U. S. Army, retired, New York City; Vanderbilt University School of Medicine, Nashville, Tenn., 1900; veteran of World War I; entered the regular Army in 1902 and retired Aug. 18, 1920, for disability in line of duty; died in the U. S. Army Hospital, Fort Jay, N. Y., July 21, aged 82.

Claudy, William Duvall Ⓜ Arlington, Va.; George Washington University School of Medicine, Washington, D. C., 1938; member of the board of police and fire surgeons of the District of Columbia; certified by the National Board of Medical Examiners; served an internship at George Washington University Hospital and served a residency at the Gallinger Municipal and Doctors hospitals in Washington, D. C.; major in the medical corps, U. S. Air Force Reserve from May, 1953, to April, 1955; died Oct. 6, aged 45.

Fischer, Andrew Leroy Ⓜ Hoffman, Ill.; American Medical College, St. Louis, 1905; past-president of the Clinton County Medical Society; veteran of World War I; during World War II received honorable mention for distinguished service as a selective service medical examiner; for many years company physician and surgeon of the Southern Railway System; in 1951 the people of Hoffman presented him with a plaque "in appreciation of 45 years of faithful service to the village of Hoffman and Community"; on the staffs of St. Joseph's Hospital in Breese and St. Mary's Hospital in Centralia, where he died Sept. 28, aged 77.

Harrison, Ross Granville, New Haven, Conn.; born in Germantown, Pa., Jan. 13, 1870; received the degree of doctor of philosophy at Johns Hopkins in Baltimore in 1894 and the medical degree at Rheinische Friedrich-Wilhelms-Universitat Medizinische Fakultat, Bonn, Prussia, 1899; lecturer in morphology at Bryn Mawr (Pa.) College, 1894-1895; instructor and associate in anatomy at Johns Hopkins from 1896 to 1899 and associate professor of anatomy from 1899 to 1907; from 1907 to 1927 Bronson Professor of Comparative Anatomy at Yale University and Sterling Professor of Biology from 1927 to 1938, when he became professor emeritus; lectured throughout the world, having given the Dunham Lectures at Harvard University, the Croonian Lectures of the Royal Society in London, the Linacre Lectures at St. John's College, Cambridge, and the Silliman Lectures at Yale; chairman of the National Research Council in Washington, D. C., from 1938 to 1946; a member of the science committee of the National Resources Planning Board from 1938 to 1943; member of the board of trustees, Marine Biological Laboratory, Woods Hole, Mass., London Biological Station, Woods Hole Oceanographic Institute Science Service, and the Bermuda Biological Station, of which he was treasurer from 1930 to 1946; past-president of the sixth Pacific Scientific Congress, American Society of Zoologists, American Association of Anatomists, Anatomische Gesellschaft, and the American Society of Naturalists; fellow of the American Association for the Advancement of Science and the American Academy of Arts and Sciences; member of many national, state and local professional and scientific societies; member, honorable member, corresponding member, or foreign member of several foreign professional and scientific societies; for many years member of the board of scientific directors and trustee of the Rockefeller Institute for Medical Research; member of the board of scientific advisers, Jane Coffin Childs Fund for Medical Research; in 1956 recipient of the Antonio Feltinelli award of the Accademia Nazionale dei Lincei, Rome, Italy; in 1914 awarded the Archduke Rainer Medal of the Imperial Royal Zoological Botanical Society of Vienna; in 1925 given the John Scott Medal and premium by the city of Philadelphia "for the invention of devices for tissue grafting and for tissue culture"; in 1947 awarded the John J. Carter Medal of the National Academy of Sciences; in 1907 was the first to adapt the hanging drop culture method to the study of embryonic tissues and demonstrated directly the outgrowth of the developing nerve fiber; member of the editorial board, and from 1903 to 1946 managing editor of the *Journal of Experimental Zoology;* held honorary doctor of science degrees from the universities of Cincinnati, Chicago, Columbia, Dublin, Harvard, Michigan, and

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Ⓜ Indicates Member of the American Medical Association.

Yale; also held an honorary M.D. degree from Pazmany University, Budapest, an honorary Ph.D. from the University of Freiburg, and an honorary LL.D. degree from Johns Hopkins University; died Sept. 30, aged 89.

Jamison, William Parks, Rowlesburg, W. Va.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1940; veteran of World War I; died Sept. 28, aged 59.

Kalvin, Henry Maximilian Ⓜ St. Petersburg, Fla.; University and Bellevue Hospital Medical College, New York City, 1900; formerly practiced in Brooklyn, where he was on the staff of the Shore Road Hospital; died Oct. 3, aged 81.

Kimball, Russell Cornelius, West Brentwood, N. Y.; University of Michigan Medical School, Ann Arbor, 1928; member of the staff of the Pilgrim State Hospital; died July 7, aged 58.

Lane, Andrew J., Detroit; University of Louisville (Ky.) Medical Department, 1909; veteran of the Spanish-American War; died Aug. 2, aged 86.

Lang, John Michael Ⓜ Del Mar, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; formerly assistant professor of obstetrics and gynecology at his alma mater; for many years practiced in Chicago, where he was on the staff of the West Side Hospital; died in La Jolla Oct. 6, aged 87.

McGuire, Lee Wesley Ⓜ Batavia, Ohio; Medical College of Ohio, Cincinnati, 1906; for many years served in the regular U. S. Navy, resigning with the rank of lieutenant commander; held the Navy Cross; formerly practiced in Boston; at one time associated with the Malden (Mass.) Hospital; died in the Jewish Hospital, Cincinnati, Oct. 1, aged 76.

Mittelmann, Bela Ⓜ New York City; Deutsche Universitat Medizinische Fakultat, Prague, Czechoslovakia, 1922; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychoanalytic Association, American Psychosomatic Society, American Psychiatric Association, and the Association for Research in Nervous and Mental Disease; visiting professor at the Albert Einstein College of Medicine; on the staff of the Bronx Municipal Hospital Center; coauthor of "Principles of Abnormal Psychology"; died Oct. 4, aged 60.

Powers, Vernon Blank, San Marco, Texas; Barnes Medical College, St. Louis, 1907; died in Austin Sept. 29, aged 75.

Roberts, C. A., Leary, Ga.; Louisville (Ky.) Medical College, 1892; died Sept. 22, aged 87.

Saylor, Clinton Theodore Ⓜ Rockwood, Pa.; Eclectic Medical Institute, Cincinnati, 1908; formerly member of the Rockwood school board and coroner of Somerset County; served on the staff of the Somerset (Pa.) Community Hospital; a charter member and past-president of the Rockwood Rotary Club; died in the Casualty Hospital, Washington, D. C., Sept. 21, aged 78.

Smith, Clarence Vernon Ⓜ Detroit; University of Illinois College of Medicine, Chicago, 1913; veteran of World War I; on the staffs of the Saratoga General and Holy Cross hospitals; died Sept. 18, aged 69.

Spinning, Alva L. Ⓜ Palm Springs, Calif.; Medical College of Indiana, Indianapolis, 1891; formerly practiced in Covington, Ind., where he was health commissioner of Fountain County; died in the General Hospital of Riverside County, Arlington, Sept. 30, aged 93.

Swanljung, Helvi Annikki, La Crosse, Wis.; Helsingfors Universitet Medicinska Fakulteten, Helsingfors, Finland, 1946; served on the staff of the Lutheran Hospital; died Sept. 30, aged 43.

Thomas, John Henry Ⓜ South Orange, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1927; certified by the National Board of Medical Examiners; member of the American Academy of General Practice; veteran of World War II; on the staff of the Orange Memorial Hospital, where he died Oct. 3, aged 55.

Vermeer, Weyer Losecaat, Upper Nyack, N. Y.; Rijks-Universiteit te Leiden Faculteit der Geneeskunde, Netherlands, 1956; served a residency at the Mount Sinai Hospital in New York City, Rehabilitation Hospital in West Haverstraw, N. Y., and the Bellevue Hospital Center in New York City; died in the Phelps Memorial Hospital, Tarrytown, Sept. 25, aged 36.

Wegener, Karl Frederick Ernest, Lincoln, Neb.; Chicago College of Medicine and Surgery, 1915; member of the American Psychiatric Association; retired from the Veterans Administration on Dec. 31, 1953; veteran of World Wars I and II; on the staff of the Lincoln State Hospital; died in Omaha Sept. 29, aged 75.

Winder, Harriet Owen, Ann Arbor, Mich.; University of Michigan Medical School, Ann Arbor, 1933; died Sept. 24, aged 51.

Zacher, Andrew Arthur Ⓜ Geneva, N. Y.; University of Buffalo School of Medicine, 1931; member of the American Society of Anesthesiologists, Inc.; died in Rochester July 28, aged 56.

Zeh, Merlin Jay, Watervliet, N. Y.; Albany (N. Y.) Medical College, 1889; also a pharmacist; served on the staff of St. Mary's Hospital in Troy; died in the Leonard Hospital in Troy Sept. 26, aged 92.

FOREIGN LETTERS

AUSTRIA

High Energy Radiation of Cancer.—At the joint meeting of the International Atomic Energy Agency and the World Health Organization in Vienna, it was reported that high energy radiation used in the treatment of malignant tumors can be either in the form of gamma rays, x-rays, or beams of accelerated electrons. The required gamma radiation can be obtained from large sources of radioactive materials, such as cobalt-60 (Co^{60}) or cesium-137 (Cs^{137}), while electron beams are produced by high-voltage accelerators. The experts considered the sources in four broad categories: large supervoltage units, intermediate units, small isotope units, and units of electron beams or high energy x-rays. The first group includes supervoltage x-ray units in the range of two to six million electron volts and Co^{60} units in which the radioactivity is of the order of 1,000 or more. These sources are kept at a minimum distance of 75 cm. from the tumor to be attacked. Intermediate units were defined as smaller cobalt units working at source-to-tumor distance in the range of 35 to 50 cm. The group believed that such units were not as good as the larger units. The only reason for their adoption would be one of economy. As regards small isotope units working at a distance of 25 cm. or less, it was agreed that these were of value for the treatment of certain selected sites in the body (e. g., head and neck) and that they should be made available either in addition to or in the absence of large units. Such units may be specifically designed to hold either Co^{60} or Cs^{137}.

DENMARK

Nickel Eczema.—Dr. P. V. Marcussen (*Ugesk. laeger*, Sept. 3, 1959) found that although modern precautions against nickel eczema contracted as an industrial disease have been remarkably effective, the opportunities for contracting it in private life have grown with the increasing use of nickel-treated articles of domestic use. In 1935 the contact dermatitis in only 5.2% of the author's patients could be traced to nickel; this occurred in 12.9% in 1955. He estimated that there were roughly 10,000 persons with a hypersensitivity to nickel in Denmark and that to this group about 800 newcomers must be added every year. In his analysis of 621 cases he showed that nickel-fitted garters were to blame in 406, tools and instruments in 57, wrist watches in 55, spectacles in 47, necklaces in 39, and aspirators, rings, telephones, or water taps in 17. In about 80% the primary eruption was soon followed by a secondary pruriginous or eczematous eruption. The eczema relapsed in 118 of the 621 patients, and as sensitivity to eczema is lifelong. the greatest care must be taken to prevent contacts with this metal. A ban on nickel-fitted garters should do much to prevent the disease.

Prognosis in Hodgkin's Disease.—Roos and Videbaek (*Danish M. Bull.*, vol. 6, September, 1959) studied a series of 172 patients with Hodgkin's disease treated in the period 1930-1945 and 117 treated in the period 1946-1955. The first group received x-ray treatment exclusively or in conjunction with blood transfusion. The second group had the additional benefit of therapy with cytotoxic agents, antibiotics, ACTH, and corticosteroids. The five-year survival rate for the first group was 33%, whereas it was 41% for the second group. Although this difference is statistically significant the authors' findings do not tally with those of other observers.

ECHO 9 Virus Meningitis.—In the latter half of 1958, 30 patients with meningitis were admitted to the Central Hospital in Herning where they were treated with antibiotics on the assumption that the disease might be of bacterial origin. Reporting on these patients Dr. S. Trier (*Ugesk. laeger*, Sept. 10, 1959) stated that six of the patients were under the age of 5 years and only six were over 20. The oldest was 47 years of age, and 21 were males. After a few days of general malaise, fever, headache, and anorexia the patients often rallied and were more or less symptom-free for four or five days, after which the temperature rose again and was associated with a violent headache, nausea, and vomiting. The fever lasted 3 to 12 days, and the meningeal symptoms disappeared promptly, with the exception of slight cervical rigidity which in some lasted for over a week. All the patients recovered, but it is doubtful if their recovery could be attributed to the antibiotics given. No bacteria could be isolated from these patients, but the ECHO 9 virus was found in 15. The cell content of the spinal fluid was much higher than is usually the case when meningitis is of viral origin, and in 12 patients more than 40% of the cells counted were polynuclear.

The items in these letters are contributed by regular correspondents in the various foreign countries.

GERMANY

The Sputum in Bronchial Cancer.—Otto and Grünbeck (*München. med. Wchnschr.* 101:1595, 1959) made sputum examinations in a series of 71 patients with bronchial cancer and compared their findings with those in aspirated samples; 44 patients had positive findings in the sputum. From 80% of a group of patients with proved bronchial carcinoma the authors found tumor cells in the sputum. In several patients the sputum examination proved superior to the examination of the bronchial secretion. Contrary to the authors' previous opinion this indicated that examination of the sputum is just as useful for diagnosis as bronchial aspiration.

Mucoviscidosis in Adults.—Koch and Lapp (*Medizinische* 24:1149, 1959) stated that mucoviscidosis (also known as fibrocystic disease of the pancreas) was formerly regarded as a hereditary disease, with a severe and rapidly fatal course, which was found only in children. Bohn and co-workers were the first to show that the disease is even more common in adults than in children. Koch and Lapp reported the clinical and pathological findings in three men who died in their 44th, 51st, and 66th years respectively. Clinically all three patients had a chronic, recurrent bronchitis with bronchiectasis, emphysema, and cor pulmonale. The cor pulmonale was the immediate cause of death. All three patients also suffered from excretory pancreatic insufficiency, with dissociation of the enzymatic concentrations and fatty stools, for years or even decades. The resultant malabsorption had given rise to tetany, osteoporosis, hypoprothrombinemia, and symptoms of pellagra. Two patients had florid duodenal ulcers. In addition an increased sodium chloride excretion in the sweat with hyponatremia and hyponatriuria could be demonstrated in all three patients. Autopsy revealed increased mucus secretion in the region of the bronchiectatic cavities, viscous mucous plugs in the mucous glands of the gastrointestinal tract, and fibrous changes in the pancreas. These findings corresponded to those of mucoviscidosis but were much less marked than in the childhood form of the disease.

Nephrosis.—Acker and Schreier (*München. med. Wchnschr.* 101:221, 1959) said that the expectation of success in the treatment of nephrosis in children has increased greatly since the introduction of sulfonamides, antibiotics, and cortisone. In the Heidelberg clinic about 75% of patients with genuine nephrosis were cured, whereas in those with an added element of nephritis the mortality was about 50% and it was doubtful whether the remaining 50% would completely recover. The basis of treatment remains a protein-rich, salt-free, low-fat diet. In addition there are various diuretics, which, however, produce only a transient diuresis and this in only a few patients. Substances which raise the colloid osmotic pressure of the blood had a variable effect; with human albumin the excretion of protein rose markedly. Cation exchange resins and elimination of focal sepsis produced no improvement in the clinical findings.

In two patients with genuine nephrosis, infection with measles seemed to have a good effect, but in eight others infection with measles was unsuccessful. Other intercurrent infections produced an increase in the proteinuria. Use of tibione and hyaluronidase had little or no effect. Long-term drainage of the ascites or kidney decapsulation also produced no change in the clinical findings. Sulfonamides and antibiotics saved lives by combating bacterial infections which had previously accounted for most of the deaths among children with chronic nephropathies. Undoubtedly treatment with prednisone and ACTH should at least be given a trial in patients with pure nephrosis.

Tetanus.—P. Mollaret (*München. med. Wchnschr.* 101:51-53, 1959) stated that modern methods of narcosis with purified and standardized curare preparations combined with promazine have opened up new possibilities in the treatment of tetanus. On the basis of a series of 120 patients he recommended the following principles of treatment. For mild cases with minimal generalized symptoms and no respiratory or autonomic disturbances curare, intravenous feeding, and tracheotomy are not indicated. In addition to continuous medical supervision, with quarter-hourly pulse and blood pressure readings and alteration of treatment at the first sign of deterioration of the patient's condition, he recommends treatment with bromide, chloral, diphenylhydantoin, chlorpromazine, or promethazine every four hours. Two or three of these drugs should be given at the same time. Blood CO_2 and electrolyte levels and pH should be estimated daily, and the chest should be x-rayed daily also.

For cases of moderate severity with generalized spasm, severe trismus, and dysphagia, but no fever or sympathetic or respiratory disturbances, in addition to the strictest supervision, immediate tracheotomy, intravenous feeding, and larger doses of the above-mentioned drugs are indicated. Curarization is not required. For the severest cases maximal curarization for about three weeks and artificial respiration by means of a respirator according to the volumetric principle are necessary in addition to tracheotomy and intravenous feeding. Special attention should be directed to any rise in the systolic blood pressure, slowing of the pulse rate, and sweating or chilling of the extremities. Autonomic disturbances often appear on the fourth or fifth day after the appearance of symptoms, and when this occurs blockage of the nerves with 1% procaine solution given as a subarachnoid infusion for 30 to 40 minutes at the rate of 1 cc. per minute simultaneously with intravenous injection of levarterenol has proved effective. This technique has reduced the mortality in this group by 30 to 50%.

Prevention of Sudeck's Atrophy.—L. Böhler (*München. med. Wchnschr.* 101:663, 1959) stated that treatment of injuries or inflammation with plaster of paris often results in disturbances of circulation which give rise to Sudeck's atrophy. In this condition there is a rise in skin temperature, edema, and pain. Later trophic skin lesions and disturbances of growth of fingernails and toenails occur. Women over 40 years of age are not often affected. The author insists on the necessity of splitting the plaster immediately after its application, and on the importance of beginning active exercises immediately. With such treatment only four cases of Sudeck's atrophy occurred among 15,000 fractures of the radius. Primary treatment with vasodilators or cortisone instead of splitting the plaster and active exercises is contraindicated. Once Sudeck's atrophy has recurred, however, corticoids are of value.

Effect of X-rays on Cancer Cells.—O. Warburg (*Naturwissenschaften* 46:25, 1959) drew an important therapeutic inference from the theory that the source of energy in cancer cells is not respiration, as in normal cells, but fermentation. The normal growth of body cells is a strictly aerobic process, which is upset by the least depression of respiration. The growth of cancer cells, on the other hand, is partially anaerobic. Normal cells must be grown in the body. If, for instance, fibroblasts from the heart are cultivated outside the body by Carell's method for any length of time they no longer exhibit normal metabolism but show the fermentative metabolic habit of cancer cells. The cells growing in vitro are no longer normal cells but are cancer cells or cells in the process of turning into cancer cells. In vitro culture answers the question: Which came first, the fermentation or the cancer? Fermentation takes priority, for the cells growing wild in vitro by the fermentative process are not cancer cells to start with, since on reinjection into the experimental animals they do not continue to grow.

The typical cancer metabolism consists not only in excessive fermentation but also in insufficient respiration. The fall in respiration follows the increased rate of fermentation. An important factor is the decrease in the level of catalase, a respiratory enzyme which splits hydrogen peroxide into water and oxygen. Cancer cells have a low catalase content—one result of their anaerobic habit. The authors demonstrated that as a result of their low catalase content cancer cells are more sensitive than normal cells to hydrogen peroxide. If equal quantities of H_2O are given to cancer cells and normal embryonal cells, the metabolism of the cancer cells ceases after an hour while that of the embryonal cells is completely unaffected. Since it is known that x-rays give rise to hydrogen peroxide in water in the presence of oxygen, it was only a step to the idea that x-rays, which are the most effective treatment for cancer known to modern medicine, must exert their injurious effect on cancer cells simply by means of H_2O_2 and selectively at that since cancer cells contain less catalase than normal cells.

The proof of this theory was conducted along two lines. If chemically pure catalase is added to the cancer cells in small quantities prior to irradiation then their sensitivity to x-rays is greatly diminished. Other experiments showed that a given dose of irradiation could be completely replaced by the corresponding dose of H_2O_2. This is unequivocal proof that the effect of x-rays depends on the formation of H_2O_2. Red blood corpuscles are rich in catalase. For this reason it is important to eliminate red blood cells from the cancer as far as possible while it is being irradiated, since otherwise the catalase from the erythrocytes makes the cancer cells more resistent to x-rays. The irradiated parts must therefore be perfused with some fluid which is free of red blood cells but still contains an excess of oxygen—no easy problem but one which, in the present state of perfusion technique, is not insoluble.

Tuberculosis in Multiparas.—L. Mattern (*Tuberkulosearzt* 13:45, 1959) studied a group of 276 women who had had one or more confinements while suffering from pulmonary tuberculosis. Of these, 96 (34.78%) showed no change in their tuberculosis during pregnancy and the puerperium, 96 showed some improvement, 24 (8.77%) showed a deterioration in their condition, and 60 (21.73%) discontinued treatment. The incidence of exacerbations during pregnancy or in the puerperium was no higher in these women than among primigravidas. Of the total number, an exacerbation of tuberculosis which was present before pregnancy was observed in 12.03% (during the first trimester) and in 7.9% in the puerperium. Tuberculosis was first discovered during pregnancy in 6.97%. In more than 50% the pregnancy had no apparent effect on the tuberculosis.

SWEDEN

Influenza Virus in Cattle.—Investigations at the Swedish Institute of Veterinary Medicine, by K. Bakos and co-workers, of a disease among cattle showed that the virus causing this disease was identical with that causing parainfluenza 3 in human beings. The cattle disease was especially prevalent in northern Sweden and appeared in two main forms, one with intestinal and one with respiratory symptoms. It was thought that parainfluenza 3 might be the primary cause of the so-called transport disease, an infectious disease which has been found among cattle in the United States and the cause of which had been believed to be a Pasteurella.

Relationship Between Measles and Distemper.—Comparative studies between the distemper virus and the measles virus were made by Dr. Gun Carlström of the Karolinska Institute. She found that human beings who have had measles have antibodies against distemper and that injection of distemper virus in animals was followed by immunity against measles as well as against distemper. Comparisons between the two viruses showed that in spite of some differences they were closely related.

Sweden's Largest Hospital.—The recent inauguration of the central complex of the Sahlgren Hospital in Gothenburg, which is to serve as the teaching hospital of the University of Gothenburg, marks the peak of a 10-year rebuilding program. It makes the Sahlgren complex the largest hospital in Sweden (2,000 beds), and its technical planning and equipment is of a standard probably unequalled in the world. One of its most striking features is its battery of 26 operating rooms, all provided with two operating tables, so that there need be no time wasted between operations. Anesthesia is induced in special rooms, one for each operating room. A high degree of automation has been achieved in the x-ray department which is equipped to handle 60,000 examinations a year with fewer technicians than formerly required. The blood center has about 16,000 registered blood donors and can collect 100 donations a day. The serology department makes almost as many cross-matching tests. The air in the operating rooms is fully renewed every six minutes. All equipment, as well as the floors, has been made electricity-conducting. The oxygen, compressed air, and anesthetic gases are administered from a central depository in the basement and connected with the operating rooms by means of a pipeline system which has convenient wall outlets.

UNITED KINGDOM

Prince Philip, President of the British Medical Association.—Prince Philip, Duke of Edinburgh, was installed as the President of the British Medical Association. The ceremony should have taken place in July at the Annual Meeting of the Association in Edinburgh, but was delayed owing to the presence of Prince Philip and the Queen in Canada. Among those present were Sir Arthur Porritt, the president-elect; Sir Arthur Thomson, the retiring president; Dr. E. Kirk Lyon, deputy president of the Canadian Medical Association; and Dr. Louis Orr, president of the American Medical Association. After being installed as president, Prince Philip delivered an address in which he referred to the BMA as a bulwark of freedom and democracy and complimented it on the useful work that it was doing for the medical profession.

Medical History Faculty Founded.—A Faculty of the History of Medicine and Pharmacy was founded under the auspices of the Worshipful Society of Apothecaries of London. Its aim is to extend interest in medical history. No such body has hitherto existed in Britain. There are endowments for three lectureships and a research fellowship is endowed by the Wellcome Trustees.

New Research Center.—A new research center costing 2.1 million dollars was opened in Nottingham by Boots Pure Drug Co. Ltd., the manufacturing chemists and retail pharmacists. There are 24 laboratories for research in pharmacology and chemotherapy and for analytical and control work in the bioassay and microbiology divisions of the company's standards department. There is also a library of 25,000 volumes in the building, a lecture theater seating 200, and a radioactive isotope unit.

Working After Sixty-Five.—In Britain a number of men continue to work after the pensionable age of 65, most of them from economic necessity. How many are really fit to continue working after this age has never been ascertained. Edwards and co-workers investigated the question with the help of a team of Birmingham general practitioners (*Brit. J. Prev. Med.* 13:51-59, 1959). In a survey made of the health of a sample of men over 70 years of age it was found that the main causes of illness were bronchitis, ischemic heart disease, and arthritis. Hypertension, hernia, and peptic ulcer were also prevalent, although they caused much less disability. With the exception of bronchitis, the incidence of these conditions was unaffected by social class. Arthritis was the only disease that increased in frequency with advancing years.

Fitness for work in the elderly man depends not only on his health but also on the nature of his work. Of the men over 70 years of age in social class 1 (professional class) 67% were considered to be fit for full-time work, and of these 33% were working. By contrast only about 20% of the men in social class 5 (unskilled workers) were passed as fit for their particular type of employment. In spite of this many were still working because of sheer economic necessity. The difference in fitness in the professional and unskilled classes was largely due to the high prevalence of chronic bronchitis in the latter. The men were also questioned about their pursuits. Gardening was the chief one. Most of the men had a good appetite and enjoyed their food. About 67% were under some form of medical supervision, but only 5% required active medical or surgical treatment; 7% were sufficiently disabled to need assistance with washing, dressing, and eating. About 50% required domestic help.

Shortage of Dietitians.—The British Dietetic Association has set up a fact-finding committee of members to inquire into the shortage of dietitians, particularly in the National Health Service. The committee's interim report says that a request was sent to hospital management committees and boards [illegible] governors of teaching hospitals asking for infor[illegible]tion on the employment of dietitians. In 100 [illegible]oups of hospitals no dietitians were employed. In 314 hospital groups with 391 positions available as full or part-time dietitians and catering officers, only 279 were filled. As the number of students qualifying each year as dietitians is about 45, the shortage is likely to continue.

Hospital Accident Services.—The British Orthopedic Association states, in a memorandum on accident and casualty services, that in certain areas hospital accident services are a blot on the National Health Service. As a result of the memorandum representatives of the Royal Colleges of Surgeons of England, Edinburgh, and Ireland, the Royal Faculty of Physicians and Surgeons, Glasgow, and the College of General Practitioners will meet to discuss the problem. Mr. H. J. Seddon, president of the British Orthopedic Association, said in a press interview that an advisory team will be set up to visit the various areas. The broad outline of the scheme being considered is to reduce the numbers of hospitals to which casualties are taken and to have an around-the-clock accident service at certain designated hospitals only. At present, persons involved in accidents may be sent to any hospital where expert treatment for the particular injury sustained may or may not be available. In London, although there are over 100 hospitals where casualties may be taken, few are fully equipped to deal with serious accident cases. The result is that treatment is delayed because the patient must be transferred to another hospital, or if treatment is given it is not the best. The new scheme would equip 20 to 30 hospitals to deal with any accident, however severe, and to give the best possible treatment.

Mr. Seddon said that two types of hospital were envisaged. There would be a centrally located general hospital, preferably a teaching hospital, which would have an accident unit with all its facilities and specialist staff, including orthopedic, plastic, general, and neurosurgical, who would be available at all hours of the day. The unit would have its own pathological and radiographic service and its own operating suite. A "flying squad" would be ready to go to any hospital of the second type situated in the periphery. Peripheral hospitals would receive and treat casualties and would refer only serious or complicated cases to the central hospital. The chief of the accident unit need not necessarily be an orthopedic surgeon, although most accidents come within this field and the scheme need not require increased staff, only reorganization.

Dr. James Fairley, the Southeast Metropolitan Regional Hospital Board's senior medical officer, objected on the ground that it is not practicable to reserve 150 to 250 accident beds for each 500,000 of the population as suggested. Even the large London hospitals could not do this, as at any one time a number of these would be empty. He suggested that the central hospitals might give the initial specialist treatment, and then if there is pressure on bed space, the patients could be transferred to convalescent units. At one center that has been set up the period of hospitalization for minor accidents has been reduced from 21 to 5 days.

Factory in a Mental Hospital.—Eighteen months ago factory work was started in Goodmayes Mental Hospital, Ilford, Essex. The object was to provide some form of activity for the patients and remuneration to add interest to the work. The scheme was so successful that it was expanded to provide paid work for about 150 patients. Originally 36 chronic, refractory, and deteriorated mental patients, most of whom were schizophrenic, were found working, although they were not compelled to do it. They were given mica to split and sort. Simple jigs and equipment were provided for the work. Payment was based on output, and when this could not be conveniently estimated the output of a team was calculated. The patients have split 750 kg. of mica, made 150,000 boxes and 10,000 carrier bags, stuck 44,000 labels, painted several hundred toys, and counted and bundled millions of punched-out cardboard shapes from which boxes are made. In the first year these patients earned $870. The rates of pay are low, but the money provides an interest and incentive.

After a year's employment in the hospital the average patient slept better; was less restless, talkative, and aggressive; worked with less supervision than at the conventional hospital occupational therapy; and was more cooperative and friendly. About 75% of the patients judged on these criteria were improved and the rest unimproved or worse. The latter group were passive, inert, and lacked the will to do anything, but few patients now sit idly about, and quarrels between the patients are infrequent as most of them are too occupied with their work. Arrangements were made for selected patients to go to factories outside the hospital to work for short periods under protected conditions.

CORRESPONDENCE

BIZARRE INTOXICATIONS

To the Editor:—In The Journal, Nov. 7, page 1342, Green's paper on nutmeg poisoning is timely, in that, along with plastic "glue glugling" and gasoline sniffing, Myristica fragrans is being used by teen-agers and perhaps even smaller fry as the means for achieving intoxication inexpensively. The taking of nutmeg mixed with water, an old practice among narcotics addicts, was reported in *Today's Health*, October, 1959, page 78, and on one occasion I saw some teen-agers "spike" their beer with it. Although I have had no nutmeg addicts as patients, I have seen about every other kind. Of special interest at the moment is a 6-year-old child, who was brought to my office recently so inebriated he could not stand. His mother said that he had been addicted to sniffing gasoline for 18 months. I would appreciate hearing from other physicians who have seen similar patients. The inhalation of gasoline fumes seems to be a craze among very young children in my community at the moment.

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RECURRENT POLYSEROSITIS

To the Editor:—In The Journal, Aug. 22, page 2131, Drs. Priest and Nixon refer to the editorial in the June 6 issue, page 678, on familial periodic disease, proposing for it the name "familial recurrent polyserositis." Our experience with this disease dates back to 1946, when we reported two cases to the Jerusalem branch of the Israel Medical Association. Since then we have studied more than 50 cases. In view of the fact that the fundamental feature of the disease is a recurrent inflammation of the serous membranes, we called it "recurrent polyserositis," which is in agreement with the suggestion of Drs. Priest and Nixon. An objection might be made to the addition of the adjective "familial." It is true that familial occurrence is not infrequent, but it varies widely in different reported series and is not necessarily an integral feature of the disease. In most of the patients we have seen, only one member of the family was affected.

In 1958 we reported (*Israel M. J.* 17:150 [July-Aug.] 1958) that some patients with recurrent polyserositis exhibit marked hypersensitivity to old tuberculin. This was demonstrated by their positive skin reactions to dilutions as high as 1:100,000,000 and by the fact that attacks, indistinguishable from the spontaneous ones, could be provoked by the intradermal injection of minute amounts of tuberculin. Desensitization, carried out in two patients, resulted in remissions for as long as two years. This observation led to the assumption that the attacks of recurrent polyserositis are manifestations of a hyperergic state. The occurrence of amyloidosis in some patients is consistent with the allergic concept of the disease. Our experience in this respect is similar to that of the American authors in that we have seen only a few patients with this complication.

There is a finding which may sometimes be helpful in the diagnosis of the disease, especially in view of the paucity of physical signs in the intervals between the attacks. About 50% of the patients have colloid body-like dots in the ocular fundi (Michaelson and others: *A. M. A. Arch. Ophthalmol.* 62:1 [July] 1959). The underlying cause of this finding has not yet been established.

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DIHYDROSTREPTOMYCIN OTOTOXICITY

To the Editor:—I have read the article "Dihydrostreptomycin Deafness" in The Journal, Aug. 1, page 1657, reporting 32 cases of deafness occurring after the administration of dihydrostreptomycin or products containing this substance associated with other antibiotics. I should like to mention the possibility of the reduction of dihydrostreptomycin ototoxicity by the addition of pantothenic acid or sodium pantothenate. In this way we can employ the beneficial action of dihydrostreptomycin, especially in tuberculosis. Some bibliographic references are included.

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Postmortem studies were carried out in 9 patients. Three of these had had evidence of associated heart disease during life. The clinical diagnosis of cor pulmonale in 2 patients and of hypertension in 1 was confirmed at autopsy. The remaining 6 patients had auricular fibrillation and congestive cardiac failure during life, but no clinical evidence of associated heart disease. One of these 6 patients, who died of carcinoma of the rectum, showed no evidence of cardiovascular disease on autopsy. In one of the remaining 5 patients coronary atherosclerosis was present; in another patient there was slight coronary atheroma, not considered sufficient to produce the marked cardiac disturbance during life; in 3 patients moderate to marked hypertrophy of one or both ventricles existed, but no other possible etiological factor producing heart disease, apart from thyrotoxicosis, was found. Thus, in 4 of the 9 cases in which autopsy was performed, no cause of heart failure other than thyrotoxicosis was found. The authors conclude that, although thyrotoxicosis may not be the sole cause of the cardiac disability, in many patients with thyrotoxicosis and heart disease it is nevertheless the predominant factor. I^{131} therapy is safe and effective, and is the treatment of choice in thyrotoxic patients with severe cardiac complications.

Treatment of Rheumatoid Arthritis by a Sanatorium Regime: The Black Notley Experiment. R. M. Mason and W. G. Wenley. Ann. Rheumat. Dis. 18:91-99 (June) 1959 [London].

The authors report on a pilot experiment that was set up to determine whether the treatment of rheumatoid arthritis by sanatorium methods was likely to make a useful contribution to the management of this disease. For the past 4 years 10 beds for female patients, which were previously used in tuberculosis treatment at the Black Notley Sanatorium, have been made available to the authors. During this time 40 patients with severe rheumatoid arthritis were admitted for an average stay of 6½ months. They were treated along standard sanatorium lines, with prolonged rest in bed, as much out-of-doors as possible, and with suitable splinting. This group of patients had a longer duration of disease than those admitted to beds in a London hospital during the same period (an average of 9.4 years, compared with 7.5). A comparison of the sanatorium group with other comparable groups shows that they represented a more severely affected group, as measured by functional capacity and course of disease before admission, although there were no significant differences in the degree of disease activity.

At the time of discharge there was a significant improvement in the sanatorium patients in functional capacity, the proportion only partially disabled increasing from 50 to 68%, and the proportion completely incapacitated decreasing from 50 to 24%. At follow-up (average time, 17 months), further improvement in functional capacity was observed. Improvement in disease activity also took place, although this improvement was less than that in functional capacity. Severe incapacity appeared to be no contraindication to admission to the sanatorium regimen, but the functional capacity of patients with a short duration of disease improved more than that of those with a long duration of disease. This experiment suggests that sanatorium treatment of rheumatoid arthritis is worth pursuing, but that much greater emphasis should be placed on adequate rehabilitation procedures.

The Significance of Pleural Effusion. S. K. Sweany. Illinois M. J. 116:123-128 (Sept.) 1959 [Chicago].

Pleural effusion should never be regarded lightly, and every attempt ought to be made to establish the causitive etiology. The presence of pleural effusion accompanying an illness should be suspected when there is chest pain with respiratory movement. This situation demands a roentgenologic examination of the chest, which should be repeated 2 weeks later, since the first chest film may not reveal early changes. When an effusion is suspected, physical examination will support this suspicion by dulness to percussion, decreased breath sounds, and vocal fremitus over the involved side.

Tuberculosis and carcinoma are the 2 most important conditions that produce pleural effusions. An effusion appearing insidiously, especially in a young person, should be considered tuberculous until proved otherwise. Yet it is not uncommon for an effusion appearing in a person 40 years of age or older to be tuberculous. The onset may be abrupt, but usually is insidious, and often is accompanied by fatigue, weight loss, and low-grade fever. The tuberculin skin test usually is strongly positive, but it may be negative during an anergic phase. It may be wise to repeat the skin test after 2 to 4 weeks. It is important to establish the tuberculous nature of the effusion, because proper use of antituberculous chemotherapy is curative, and nontreatment results in active open disease in more than 50% of the cases within 2 years. Effusions produced by malignancies are characterized by a tendency to produce ever increasing amounts of fluid, and generally by a downhill course. They occur more commonly in the older age group and usually are insidious in onset. The character of the fluid will vary, depending upon whether there is direct invasion of the pleural space with tumor or whether the fluid is the result of dynamic pressure changes from vascular occlusion by the tumor. With direct invasion, the fluid has a higher specific gravity, is frequently bloody, and often has malignant cells in the sediment. Pleural invasion with carcinoma car-

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Use of a Combined Preparation of Penicillin, Sulfonamides and Aminopyrine in the Prophylaxis of Rheumatic Disease. C. Chierego. Policlinico (sez. med.) 66:345-357 (Aug.) 1959 (In Italian) [Rome].

A combined preparation of benzathine penicillin G, sulfathiazole, sulfisoxazole, and aminopyrine was administered as a prophylactic drug against rheumatic fever to 46 secondary school children, aged between 11 and 14 years, whose standard health questionnaires indicated a regressed or current state of rheumatic disease or suspected presence of a local (oropharyngeal) infection. Treatment was conducted for 16 months, with a 4-month drug-free period in between. The preparation was administered for 4 consecutive days a week in the form of 3 tablets a day, each tablet containing 150,000 units of benzathine penicillin G, 125 mg. of sulfathiazole, 125 mg. of sulfisoxazole, and 150 mg. of aminopyrine.

Pain in the joints, which was present in 29 pupils (63%) at the beginning of treatment, affected only 4 at the end of such treatment; tonsillar infection, which was present in 42 pupils (91.3%) at the beginning, affected only a few at the end of the treatment. The effect of the prophylaxis was evaluated objectively on the basis of the tests recording antistreptolysin titer, C-reactive protein level, and erythrocyte sedimentation rate at the beginning and at the end of each course of treatment and 3 months after the termination of the therapy (5 courses altogether). The serologic tests were carried out in those who received the prophylactic treatment and in a control group of 40 children who had a current rheumatic or tonsillar involvement but had not received the prophylactic treatment. The values of the serologic tests were above the physiological limits when the treatment began in both groups of children. These values were restored within the physiological limits in the group who received the treatment, but they remained almost unchanged in the control group at the end of the treatment. No severe side-effects to the drug were observed. A temporary episode of slight diarrhea affected 2 pupils, and slight nausea 1.

The Nature and Prognosis of Heart Disease in Thyrotoxicosis: A Review of 150 Patients Treated with ^{131}I. G. Sandler and G. M. Wilson. Quart. J. Med. 28:347-369 (July) 1959 [London].

Although the occurrence of heart disease in thyrotoxicosis is recognized, opinions are still divided about the relationship of thyrotoxicosis to the genesis of the cardiovascular abnormalities. While some authors have maintained that thyrotoxicosis alone can cause heart disease, others have claimed that associated heart disease is always present in such patients in addition to thyrotoxicosis. The authors selected for detailed study patients with cardiac involvement from among a large group of patients with thyrotoxicosis who had been treated with radioiodine (I^{131}). Evidence of heart disease was present in 150 of 462 thyrotoxic patients treated with I^{131} at 2 Sheffield hospitals between 1949 and 1956. Eighty-six of these patients had associated heart disease, comprising ischemic, hypertensive, rheumatic, pulmonary, and congenital heart disease. The remaining 64 patients had auricular fibrillation, congestive cardiac failure, or cardiomegaly alone, in the absence of any clinical, radiologic, or electrocardiographic evidence of associated heart disease. Patients with cardiac involvement were found in the older age groups. Sex, incidence of goiter, and severity and duration of thyrotoxicosis did not appear to be related to the incidence of cardiac involvement. Approximately one-third of the patients with auricular fibrillation reverted spontaneously to normal rhythm after I^{131} therapy, the most important factor adversely influencing reversion being the presence of congestive failure. The rate of reversion was higher in younger patients and in male patients.

More than half of the patients with congestive cardiac failure had no further attacks of failure after I^{131} therapy, and more than one-third required no further treatment with digitalis or mersalyl. The prognosis in patients with congestive failure and auricular fibrillation was more favorable if sinus rhythm was restored. In 13 patients without associated heart disease, there was radiologic and electrocardiographic evidence of left ventricular enlargement in the absence of auricular fibrillation and congestive cardiac failure. A return to normal did not occur after I^{131} therapy.

The place of publication of the periodical appears in brackets preceding each abstract.

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Tuberculosis and carcinoma are the 2 most important conditions that produce pleural effusions. An effusion appearing insidiously, especially in a young person, should be considered tuberculous until proved otherwise. Yet it is not uncommon for an effusion appearing in a person 40 years of age or older to be tuberculous. The onset may be abrupt, but usually is insidious, and often is accompanied by fatigue, weight loss, and low-grade fever. The tuberculin skin test usually is strongly positive, but it may be negative during an anergic phase. It may be wise to repeat the skin test after 2 to 4 weeks. It is important to establish the tuberculous nature of the effusion, because proper use of antituberculous chemotherapy is curative, and nontreatment results in active open disease in more than 50% of the cases within 2 years. Effusions produced by malignancies are characterized by a tendency to produce ever increasing amounts of fluid, and generally by a downhill course. They occur more commonly in the older age group and usually are insidious in onset. The character of the fluid will vary, depending upon whether there is direct invasion of the pleural space with tumor or whether the fluid is the result of dynamic pressure changes from vascular occlusion by the tumor. With direct invasion, the fluid has a higher specific gravity, is frequently bloody, and often has malignant cells in the sediment. Pleural invasion with carcinoma carries a hopeless prognosis, but can be ameliorated with the use of nitrogen mustard and radioactive heavy metal solutions.

The value of pleural biopsy by both needle and open surgical technique is emphasized. The author discusses the results obtained from 106 needle-biopsy specimens in 88 patients. In 10 patients malignancies were demonstrated by needle biopsy. In 10 additional patients malignancies were subsequently discovered by other means from 6 months to 3 years later. Thus, in the presence of malignancies the diagnostic yield of pleural needle biopsy was 50%. Granulomatous pleuritis with giant-cell formation and sometimes caseation and acid-fast bacilli were detected by biopsy in 13 cases. Only one of these was not confirmed by finding the organism later, but even this patient responded to antituberculous chemotherapy. Thus, biopsies yielded positive diagnoses in 26% of the 88 cases. These diagnoses are obtained with minimal trauma to the patient, and with saving of both time and money in shortened hospitalization and fewer diagnostic procedures.

The Significance of Respiratory Symptoms and the Diagnosis of Chronic Bronchitis in a Working Population. C. M. Fletcher, P. C. Elmes, A. S. Fairbairn and C. H. Wood. Brit. M. J. 2:257-266 (Aug. 29) 1959 [London].

The diagnostic problem of chronic bronchitis was studied by asking 192 postmen and 192 female post-office employees of London, 40 to 59 years of age, a number of questions regarding cough, expectoration, and other symptoms, by measurement of sputum volume and of ventilatory capacity, and by inspection of sickness-absence records. The men had more cough and sputum than the women, but the prevalence of other symptoms and of chest illness was similar in the 2 sexes. Symptoms increased with age in the men but not in the women. These differences were only partly attributable to differences in smoking habits. The severity of phlegm production was graded according to whether or not it occurred throughout the day, and this grading correlated well with the volume of sputum produced in the first hour after waking. Whether or not the phlegm was said to be perennial appeared not to matter. Ventilatory capacity was significantly impaired in the men, but not in the women, who had the higher grade of phlegm production, frequent wheezing, susceptibility to adverse weather, and a history of chest illnesses with an increase of phlegm production.

The authors suggest that chronic bronchitis should be diagnosed in subjects with a productive cough not due to other causes, and that it should be graded in severity either according to the persistence of the symptom throughout the day or according to the volume of sputum expectorated. Disability from impairment of ventilatory capacity or recurrent chest illnesses should be regarded as complications, and not as essential features of chronic bronchitis, since it is important to recognize the disease before it has resulted in disability. The disabling form of the disease can be referred to as "chronic bronchitis with ventilatory impairment" and "chronic bronchitis with recurrent exacerbations" and may be graded according to the severity of the impairment and the frequency of exacerbations. Disability appears to be a less frequent consequence of chronic bronchitis in men than in women.

Bronchial Changes in Hodgkin's Disease (Malignant Granuloma). C. Dijkstra. Nederl. tijdschr. geneesk. 103:1516-1521 (July 25) 1959 (In Dutch) [Amsterdam].

On the basis of detailed histories of 3 patients, the author demonstrates that granulomatous changes may be found in the bronchi of patients with Hodgkin's disease. While ordinarily these lesions may be relatively unimportant in the over-all clinical picture of Hodgkin's disease, the cases presented illustrate that they sometimes give rise to atelectasis and pneumonitis of a part or of an entire lung and thus have a decisive influence on the course of Hodgkin's disease. One of the patients presented had tuberculous pulmonary lesions in addition to the lymphogranulomatous bronchial lesions.

Familial Hemolytic Anemia with Erythrocyte Inclusion Bodies and a Defect in Pigment Metabolism. R. Schmid, G. Brecher and T. Clemens. Blood 14:991-1007 (Sept.) 1959 [New York].

The authors report on 2 patients, a 35-year-old man and his 11-year-old son, with a congenital and familial hemolytic syndrome, which was characterized by the presence of spontaneous inclusion bodies in the erythrocytes and by the excretion of dark-brown pigments in the urine. Splenectomy did not improve the marked hemolytic anemia in either patient. The father had an acute attack of biliary obstruction due to multiple gallstones in the common bile duct. He died after a surgical attempt to relieve the obstruction. The son had an aplastic crisis, occurring in the course of a pneumonitis of undetermined causation, during which frequent transfusions were necessary to maintain an adequate hemoglobin level. Associated with this attack was a transient disappearance of the urinary pigments and a decrease in the serum bilirubin level. The patient gradually recovered, and in the fall of 1958, when this report was submitted for publication, he was leading a normal life and maintaining a hemoglobin level of about 10 Gm. per 100 cc.

Special studies at the National Institutes of Health in Bethesda, Md., revealed that the inclusion bodies present in about 33% of the erythrocytes of both patients were indistinguishable from Heinz-Ehrlich bodies. They occurred in reticulocytes and occasionally in normoblasts. In addition to these bodies, many erythrocytes contained basophilic stippled cells, siderocytic granules, and rod-like structures. These morphologic abnormalities are believed to be the result of an inherited metabolic abnormality of the red blood cells. The urinary pigments were found to have chemical and spectroscopic properties which were similar to those of mesobilifuscin. It is believed that these pigments possessed a dipyrrolic structure and were derived from erythrocyte catabolism. Transfusion of the older patient's erythrocytes into a normal recipient resulted in rapid removal of the heterologous cells from the circulation and in excretion of similar dark pigments in the urine.

The Incidence of Leukemia in Families of Patients with Hypoplasia of the Marrow. S. Garriga and W. H. Crosby. Blood 14:1008-1014 (Sept.) 1959 [New York].

The authors collected from the literature 66 cases of Fanconi's syndrome of hypoplasia of the bone marrow, involving 48 families. Among these families there were mentioned 4 cases of leukemia—2 of them in cousins, 1 in a brother, and 1 in an uncle; in one patient with Fanconi's syndrome acute leukemia developed after the patient had been ill for 4 years with hypoplastic disease of the marrow. Atrophy of the spleen is a common fault in patients with Fanconi's syndrome and may reflect a generalized dystrophy of the tissues of mesenchymal origin. The high incidence of leukemia in the families of patients with hereditary hypoplasia of the bone marrow suggests that the hereditary fault which permits development of Fanconi's syndrome may also cause a predisposition to leukemia, even among those in whom the gene is not so completely expressed as to cause Fanconi's syndrome.

Infectious Mononucleosis: A Review of 572 Cases. F. T. Lou. Chinese M. J. 79:175-177 (Aug.) 1959 [Peking].

The authors report on 572 patients with infectious mononucleosis, who were observed in the course of an epidemic in Shanghai, which reached its peak during November and December, 1954. Most of the patients were young persons, aged less than 25 years. The clinical features were comparable to those reported in the world literature, except for certain differences, such as the high incidence of an acute onset and of gastrointestinal symptoms, generalized enlargement of lymph nodes, and occurrence of parotitis and epididymo-orchitis. Treatment was essentially symptomatic; several antibiotics and sulfonamides were given a therapeutic trial, and no remarkable difference in effectiveness was found.

Serial hematological observations revealed that the total white blood cell counts generally increased during the first 2 or 3 days of infectious mononucleosis and returned to normal limits or decreased after the 3rd or 4th day. Lymphocytes were increased after the 3rd or 4th day, with the absolute counts usually varying between 3,000 and 4,000 per cubic millimeter, the highest being 12,040. Morphologically, the abnormal lymphocytes were similar to those described by Downey. The abnoral lymphocytes persisted for 2 months at least, but only rarely for more than 4 months. Serologic observations showed that titers of heterophilic agglutinins above 1:64 were found in 96.4% of the patients. The diagnosis was further confirmed by adsorption tests in 86.5%. Attempts to isolate the causative agents from the patients' blood, bone marrow, cerebrospinal fluid, urine, and feces by culture proved unsuccessful. Proliferation of lymphoid tissue and reticuloendothelial cells and infiltration of large-sized mononuclear cells were found on examination of a few specimens of lymph node, salivary gland, and liver tissue obtained from these patients.

Autopsy was performed on a patient who died of infectious mononucleosis. Scattered hemorrhages, degeneration and necrosis of parenchymal cells, and infiltrations of mononuclear cells in the liver, kidney, and adrenal cortex were seen. Multinuclear giant cells were found in several tissues. Abnormal changes of the heart, brain, stomach, and intestines were evident.

Essential Thrombocythemia: Eight New Cases, Together with Follow-up Examination of Owren's Patient. J. Deduchen, O. Refvem and K. Ytrehus. Nord. med. 62:1265-1270 (Aug. 20) 1959 (In Norwegian) [Stockholm].

Not many cases of essential thrombocythemia have been published to date. The authors describe 8 new cases of the disease in detail and include a follow-up study of Owren's case, reported in 1943. Owren's patient was found to be subjectively free from symptoms. A familial type of hemorrhagic diathesis was seen in only one instance. The time from the first marked manifestation to diagnosis ranged from 2 to 10 years, and averaged about 4 years. Up to now the duration of the disease has been from 4 to 35 years. Two patients probably died of myocardial infarction after 4 and 6 years respectively. Hemorrhage occurred in 5 patients, and thrombosis in 4, but only 3 patients had both of these symptoms. There were considerable neurasthenic disturbances in 4 patients. Essential thrombocythemia should be suspected, particularly in patients, aged 40 to 50 years and older, in the presence of one or more of the following symptoms, if they are not otherwise explained; (1) recurrent bleeding in skin, nose, mouth, and especially inner organs; (2) tendency to thrombosis; (3) enlarged spleen and/or

loss of the extremity. The alleviation of symptoms is the only indication for direct arterial surgery in these patients. More careful selection of patients for femoral bypass must be employed in the future. The risk in patients with diffuse arteriosclerosis is considerable, even for relatively minor procedures. Patients over 70 years of age will rarely be candidates for this procedure. Patients with diabetes mellitus or gangrene were rarely benefited in this series. The importance of adequate preoperative femoral arteriograms is stressed. The distal arterial bed must be shown to be patent by preoperative examination or by distal operative angiography for successful results to be anticipated. The use of serial angiographic techniques and biplane studies have been suggested as 2 methods of achieving this end. Teflon and Dacron appear to be the most promising prosthetic materials currently available. The venous autograft still appears to have a place in the femoral bypass procedure. There was a high incidence of occlusion with the Edwards-Trapp nylon graft in this series. With more careful preoperative selection, better arteriographic evaluation, more meticulous operative technique, and more reliable prosthesis, a greater number of good results may be expected in patients subjected to femoral bypass in the future.

Breast Abscess as a Threat to Surgical Units in a General Hospital. J. G. P. Hutchison. Brit. M. J. 2:277-279 (Aug. 29) 1959 [London].

Breast abscess is frequently a postpartum condition. If confinement takes place in a maternity hospital, the organism responsible, Staphylococcus pyogenes var. aureus, will most often be one of the antibiotic-resistant types prevalent there. Disease does not supervene until some weeks after the patient's discharge from the hospital. The author made a survey among 75 patients with breast abscess admitted for surgical treatment to a general hospital during 1958. Sensitivity to antibiotics, phage type of staphylococci isolated, and the patient's history before admission were studied. The majority of strains came from women confined in hospital. Only 5% of these were fully sensitive to antibiotics. Many of the strains were resistant to 2 or more antibiotics, and the phage types of the latter strains were predominantly types 80 and 52/52A/80. Conversely, in the nonpuerperal group the majority of strains were fully sensitive, and no strain was resistant to 2 or more antibiotics. The author believes that patients with puerperal breast abscess should be removed from maternity hospitals to infectious disease hospitals rather than be nursed on general surgical wards. A plea for notification of postpartum infections is also made. The apparent use of penicillin as the first line of defense in these cases is deprecated.

Lateral Portacaval Anastomosis for Portal Hypertension: Long Term Results in 57 Patients with Intrahepatic Portal Bed Block and 8 Patients with Extrahepatic Portal Bed Block. T. B. Patton, C. G. Johnston, C. Lyons and P. Jordan Jr. Am. J. Gastroenterol. 32:291-310 (Sept.) 1959 [New York].

The authors report on 65 patients with portal hypertension, on whom lateral anastomosis between the portal and caval systems was performed in 3 Michigan and 1 Alabama hospitals. Of the 65 patients, 57, between the ages of 11 and 70 years, had intrahepatic obstruction, and 8 patients, between the ages of 5 months and 42 years, had extrahepatic obstruction. In 52 of the 57 patients with intrahepatic obstruction, the standard lateral portacaval anastomosis was carried out. When there was portal thrombosis or when there was massive bleeding in the dissection of the portal vein, some variant of the side-to-side anastomosis was carried out. In the presence of caudate lobe hypertrophy it is unwise to resect this lobe and so sacrifice functioning parenchyma or to accept the risk of bile fistula. An acceptable alternative would seem to be the use of the superficial femoral vein as a free graft between the portal vein and the inferior vena cava. This was necessary in only one patient.

Of the 8 patients with extrahepatic obstruction, 5 had the standard lateral portacaval anastomosis, 2 had a side-to-side anastomosis between the superior mesenteric vein and the inferior vena cava, and 1 had an anastomosis between the omental vein and the right renal vein. Five of the 8 patients were children, and because of the small size of the vessels available for anastomosis, the anastomosed vessels did not remain patent after construction of a shunt. Transesophageal ligation is the procedure of choice in infants and young children for the control of bleeding esophageal varices. Repeated ligations may be necessary before the patient reaches the age of 10 years. Transesophageal ligation may also be of value when a previously performed shunt has closed.

In the group with intrahepatic obstruction, there were 11 deaths in the immediate postoperative period. Autopsy was performed on 3 patients, and all had shunts which were patent and free of clot. Nineteen patients died within 41 days to 91 months after the operation. Autopsy was performed on 8; the shunts were patent and free of clot in 6, and in 2 the shunts were closed. There were 8 deaths from hepatic coma in the immediate postoperative period, and coma occurred later in 15 cases. The earlier statement in a previous report that there is less incidence of hepatic coma after lateral portacaval anastomosis must be regarded as erroneous. Hepatic coma is a problem only in patients with cirrhosis. Of the 15 patients with late coma, 9 continued to drink heavily and died in coma without evidence of recurrent esophageal bleeding. The remaining 6 liver; (4) neutrophil leukocytosis; (5) increased number of megakaryocytes in the bone marrow; (6) parestheses (including restless legs); and (7) slight proteinuria accompanied by increased uric acid in serum. Several cases illustrate the importance of having the possibility of essential thrombocythemia in mind.

SURGERY

Stereotactic Surgery in Parkinson's Disease. R. H. Strassburger and L. A. French. Minnesota Med. 42:1214-1218 (Sept.) 1959 [St. Paul].

The authors report on 14 patients, between the ages of 41 and 70 years, with Parkinson's disease of from 3 to 38 years' duration, who underwent stereotactic surgery at the University of Minnesota Hospitals in Minneapolis. The term "stereotactic surgery" is used for the surgical technique in which circumscribed, destructive lesions are placed in subcortical ganglions or pathways with negligible injury to adjacent structures. This is accomplished through the use of electrodes whose placement in the depths of the brain are precisely determined by mechanical guides. The first stage of the Spiegel-Wycis method of stereotaxis, adapted and employed in this group of patients, was carried out with the aid of general anesthesia and was devoted to obtaining accurate roentgen-ray studies necessary for the localization of the intracerebral target. The second stage was conducted with the aid of local anesthesia and was devoted to study of the target area by means of stimulation and observation of the clinical response patterns of evoked potentials, and destruction of the globus pallidus by coagulation with direct, anodal current.

Four of the 14 patients obtained excellent results, with 95% or better reduction of both tremor and rigidity. Five patients obtained good results, with 66% reduction of these symptoms. Three patients obtained fair results, with 33 to 66% reduction of symptoms. The 2 remaining patients were therapeutic failures, one because of permanent hemiparesis, and the other because of death which occurred 2½ weeks postoperatively after a pulmonary embolus. The age of the patients and the duration of the disease, while undoubtedly influencing the results of surgical treatment, did not necessarily preclude satisfactory results, since a 70-year-old patient obtained excellent results, and 4 patients with symptoms of 20 years' or more duration obtained either good or excellent results.

There are 4 distinct advantages to stereotactic surgery, utilizing the described technique: 1. It is an exceedingly accurate method. Destructive lesions of known size can be placed in a predetermined place with a minimum of damage to surrounding structures. 2. Before any destructive lesion is made, it is possible to carry out electrostimulation. This has the advantage of a physiological demonstration of the position of the electrode. 3. There is precise control over the size of the destructive lesion made. One coagulation produces an ovoid area of destruction of about 4-by-2-mm. size. Six to 22 lesions have been produced in various patients, the end-point being the desired clinical effect rather than an arbitrarily chosen number. 4. Reapplication of the stereoencephalotome in a precisely identical position is a simple matter. Therefore, one is able to produce further lesions at intervals, should this prove necessary. Reapplication of the instrument has been necessary in a few patients at intervals of up to 6 months, and it has been possible to do so without the need for repeat pneumoencephalography. It is felt that more data must be accumulated in order to evaluate properly the place of surgery in diseases of abnormal movements.

An Evaluation of the By-pass Graft in Arteriosclerotic Occlusive Disease of the Femoral Artery. E. F. Bernstein, J. C. Rosenberg and A. P. Thal. Minnesota Med. 42:1237-1242 (Sept.) 1959 [St. Paul].

The authors report on 29 men and 10 women, between the ages of 40 and 90 years, on whom 42 femoropopliteal bypass grafts were performed for arterioslcerotic occlusive disease of the femoral artery in the department of surgery of the University of Minnesota Hospitals in Minneapolis. Of the 42 bypass procedures, an autogenous saphenous vein was utilized for the shunt in 18, and Edwards-Trapp crimped nylon prosthesis in 23, and an Ivalon graft in 1. All the patients were followed either until failure was evident, or for a minimum period of 12 months of palliation, which was arbitrarily chosen as sufficient to justify the procedure inasmuch as these patients were operated on either for the alleviation of symptoms or to postpone amputation. There were 3 operative deaths (7.1%). Nineteen of the 39 patients had 12 months of symptomatic relief after their operation which, therefore, was considered successful. Fifteen of the 19 patients continued to have evidence of patent graft to date; in the other 4, evidence of graft failure developed subsequently, 12, 15, 19 and 23 months after the operation. The remaining 20 patients were classified as graft failures during the first postoperative year. Nine patients were subjected to major amputations after femoral bypass on the same extremity. It is significant that, whereas the greatest number of failures occurred during the first 3 postoperative months, there was a gradual increase in the failure rate through the first postoperative year.

Arteriosclerotic occlusive disease of the femoral artery is a slowly progressive condition which may lead to claudication, gangrene, and the occasional loss of the extremity. The alleviation of symptoms is the only indication for direct arterial surgery in these patients. More careful selection of patients for femoral bypass must be employed in the future. The risk in patients with diffuse arteriosclerosis is considerable, even for relatively minor procedures. Patients over 70 years of age will rarely be candidates for this procedure. Patients with diabetes mellitus or gangrene were rarely benefited in this series. The importance of adequate preoperative femoral arteriograms is stressed. The distal arterial bed must be shown to be patent by preoperative examination or by distal operative angiography for successful results to be anticipated. The use of serial angiographic techniques and biplane studies have been suggested as 2 methods of achieving this end. Teflon and Dacron appear to be the most promising prosthetic materials currently available. The venous autograft still appears to have a place in the femoral bypass procedure. There was a high incidence of occlusion with the Edwards-Trapp nylon graft in this series. With more careful preoperative selection, better arteriographic evaluation, more meticulous operative technique, and more reliable prosthesis, a greater number of good results may be expected in patients subjected to femoral bypass in the future.

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There were no deaths in the group with extrahepatic obstruction. Two of these 8 patients have bled again, and 2 of the survivors in the group with intrahepatic obstruction (both with cirrhosis of the liver) had recurrent episodes of bleeding. Two survivors in the group with intrahepatic obstruction are living and well 9 and 10 years postoperatively. Apart from technical considerations, it is impossible to identify a clinical advantage for the lateral portacaval anastomosis. Chronic alcoholism and progressive liver disease cause early demise regardless of the type of shunt performed.

Spontaneous Costal Fracture. F. A. Sanguinetti, J. Spatola and E. A. Mettler. Prensa méd. argent. 46:791-793 (March 27) 1959 (In Spanish) [Buenos Aires].

As a rule, costal fractures are caused by thoracic trauma, either direct or indirect. They immediately produce pain, which increases on palpation. Multiple spontaneous fractures of the ribs are rare, especially in man. They are more frequent on the anterior or lateral surfaces of the lower left ribs, near the cartilages, than at any other location. They do not cause symptoms and are found only during routine examination of the chest. They occur as a result of violent respiration, cough, awkward movements, or during parturition. Secondary factors are pulmonary tuberculosis, pulmonary emphysema or any other pulmonary infection, fragility of the bones from old age, osteoporosis, and diffuse diseases of the bones.

A 62-year-old man was hospitalized in an advanced stage of laryngeal histoplasmosis, pulmonary emphysema, and diffuse osteoporosis. Multiple, bilateral fractures of the posterior surfaces of the 6th, 7th, 8th, and 9th ribs occurred without any symptoms and within an interval of a few days after hospitalization. The fractures were painless, both spontaneously and on palpation, and were detected during a roentgen-ray examination of the chest. Lack of tendency to consolidate was shown both in the roentgenograms and by a biopsy specimen.

Ruptured Abdominal Aortic Aneurysm. J. A. Elliot, A. D. McKenzie and W. B. Chung. *Surgery* 46:605-617 (Sept.) 1959 [St. Louis].

The authors review observations on 28 patients with ruptured aortic aneurysm, whom they observed from January, 1956, to December, 1958. All the patients had frank ruptures with recent retroperitoneal hemorrhage. Three patients were operated on but died before completion of the procedure; in 4 no surgical therapy was attempted; and in the remaining 21 the aneurysms were resected and replaced by grafts. The majority of the patients on whom resection was performed suffered from serious coincidental disease. Thirteen were in collapse prior to the operation. Nine survived the operation for more than one month. With increase in experience the diagnosis of ruptured aneurysm was made more readily. However, physicians generally seemed to encounter difficulties, since there was considerable delay prior to the diagnosis. Ruptured aneurysm should be added to the differential list of abdominal catastrophes. Immediate operation and aortic control are the most important considerations in treatment; delay invites collapse. Other resuscitative measures have proved to be of incidental importance. The technique of the abdominal operative procedure is described.

Highlights in the experience of these authors were the use of an aortic compressor to obtain proximal control and the piecemeal excision of the aneurysm, with a protective patch left on vulnerable veins. Immediate postoperative complications were impaired leg circulation, oliguria, evisceration, other arteriosclerotic catastrophes, and mechanical obstruction of the small intestine. Two late complications of the replacement procedure were erosion of the proximal anastomosis into the duodenum and fatal gastrointestinal hemorrhage; these occurred at 6 and 33 months respectively. The homograft in the second case showed marked arteriosclerotic degeneration, and this experience as well as the availability of prosthetics, has induced the authors to prefer the latter.

Venous Thromboembolism: A Summary of 10 Years' Experience with 610 Patients and the Evolution of a Routine Management. J. N. Shadid. Surgery 46:588-604 (Sept.) 1959 [St. Louis].

The 3 important interacting factors to consider in thromboembolism are Virchow's triad of vascular damage, slowing of the blood flow, and unknown abnormalities in blood composition. While the amount of vacsular damage and stasis can be clinically estimated, no reliable index of the blood abnormalities was available. In the belief that studies of total physicochemical blood changes might provide an adequate answer, a simple bedside drop test for blood to reflect these changes was devised and applied. The experiences gained with the use of this test on 610 patients with known or *suspected venous thromboembolism* during the past 10 years indicate that its results, considered in relation to venous damage and blood flow, are trustworthy guides to lead the majority of such patients safely to recovery.

The test consists essentially in timing, under standard conditions of temperature and pressure, the interval taken by 14 drops to fall away from the tip of a standardized and sterilized test instrument containing 1 ml. of blood drawn directly into it from a vein. This drop-measuring instrument (stactometer) is made up of a 1-ml. tuberculin-type syringe barrel with a 25-gauge, ½-in. hypodermic needle attached. The blood drop time thus obtained is divided by the water drop time standard, which has been previously established for each stactometer by timing its delivery of 14 drops from 1 ml. of distilled water at 25 C. The result is the stactometric ratio (SR) and represents the combined effects of viscosity, surface tension, and specific gravity, which are reflections of the physicochemical state of the blood. Since the rate of blood dropping from the stactometer is dependent on the combined effects of the cellular and plasma elements, a hematocrit determination was performed on the same sample of blood. The test drops and the remainder of the milliliter of blood were caught in a heparinized test tube and used to provide the hematocrit figure. The SR and hematocrit of each subject were recorded on a graph. It was found that the SR line was consistently below the hematocrit line when the subject was in a state of well-being and rose above the hematocrit line when he was under mental or physical stress. This empirical relationship between the SR and hematocrit figures made the hematocrit a convenient base line along which SR fluctuations could be plotted in terms of plus or minus variations.

In all of the 610 patients a presumptive diagnosis of venous thrombosis, pulmonary embolism, or both had been made by referring physicians. Sixty of the patients could not be followed with serial determinations. A routine of management of a patient with suspected or obvious venous thromboembolism is presented. The results of this routine of management in 285 patients are recorded and are compared with the earlier results in 265 patients. It was found that the routine management (*a*) helps dispel much of the doubt from uncertain clinical situations associated with venous thromboembolism, (*b*) more definitely outlines the types and duration of treatment and safely minimizes the period of necessary observation to less than 2 weeks in 90% of the patients and indicates the need for anticoagulant therapy in only 60% of the patients, and (*c*) isolates for concentrated attention those patients requiring prolonged, meticulous treatment and those for whom new treatments should be found.

Spontaneous Hemopneumothorax. P. Bourgeois, G. Rollin and P. Dreyfus. Rev. tuberc. 23:513-532 (May-June) 1959 (In French) [Paris].

Hemopneumothorax, which is produced by the appearance, rarely simultaneous, usually successive, of air and blood in the pleural cavity, has been studied by the authors in the light of 2 cases presented in detail and 286 cases found in the literature. Spontaneous hemopneumothorax is infrequent, estimates of its incidence in relation to the total number of cases of spontaneous pneumothorax ranging from 4 to 12%. It occurs chiefly in men; only 11 cases, or about 4%, have been reported in women. More than 80% of the cases observed occurred in young men between the ages of 17 and 32 years (average, 27 years). The history revealed an occupation involving physical work or habitual participation in sports in most cases. The mortality rate has been variously estimated at from 15 to 25%, but this figure is, in fact, excessive, because, although all fatal cases are presumably reported, many mild ones are probably either not diagnosed or not published. Recovery in nonfatal cases usually takes place without sequelae of any kind within 5 to 8 weeks (3 if the condition is minimal).

Clinical evidence of hemopneumothorax is provided by a combination (with varying time relationships) of the signs of an acute respiratory disease and those of an internal hemorrhage. Spontaneous pain, the major subjective sign, usually marks the onset. It appears suddenly and is generally submammary, but may be felt in the scapular region or even in the lower thorax or below the diaphragm. The frequency of the aberrant localizations of the pain and of its atypical irradiation should be emphasized, because they may lead to serious errors in diagnosis and treatment. Dyspnea, the second essential sign, may be moderate or severe; cough is frequently present, and fever, usually not exceeding 2 degrees above normal, is almost constant. Reflex disturbances, such as nausea and vomiting, may appear, and the patient may even lose consciousness.

The signs of internal hemorrhage may pass unnoticed among the signs of the initial shock, but when they are severe, either at the outset or later on, if the condition develops in 2 stages, emergency thoracotomy may be required. Thoracotomy is also indicated when the hemorrhage persists. It is often advisable to give the patient transfusions of blood before the operation, not to gain time but to restore the blood volume to normal or nearly normal levels. Thoracotomy has many advantages; it makes it possible (1) to secure hemostasis; (2) to make an etiological diagnosis and to suppress the cause of the spontaneous pneumothorax; and (3) to evacuate all clots and thus to promote maximal functional recovery. Hemostasis sometimes occurs spontaneously in less severe cases; consequently, expectant treatment, with thoracocentesis or the insertion of a small intercostal drain for the evacuation of air and blood when the patient is seen at the very beginning of the hemopneumothorax, may be justified. The importance of surgical procedures in the treatment of hemopneumothorax makes immediate referral of patients with this condition to a thoracic surgery center advisable.

patients abandoned the use of alcohol, responded to treatment for coma, and are living and well. Of the 35 survivors, 31 are gainfully employed or going to school.

There were no deaths in the group with extrahepatic obstruction. Two of these 8 patients have bled again, and 2 of the survivors in the group with intrahepatic obstruction (both with cirrhosis of the liver) had recurrent episodes of bleeding. Two survivors in the group with intrahepatic obstruction are living and well 9 and 10 years postoperatively. Apart from technical considerations, it is impossible to identify a clinical advantage for the lateral portacaval anastomosis. Chronic alcoholism and progressive liver disease cause early demise regardless of the type of shunt performed.

Spontaneous Costal Fracture. F. A. Sanguinetti, J. Spatola and E. A. Mettler. Prensa méd. argent. 46:791-793 (March 27) 1959 (In Spanish) [Buenos Aires].

As a rule, costal fractures are caused by thoracic trauma, either direct or indirect. They immediately produce pain, which increases on palpation. Multiple spontaneous fractures of the ribs are rare, especially in man. They are more frequent on the anterior or lateral surfaces of the lower left ribs, near the cartilages, than at any other location. They do not cause symptoms and are found only during routine examination of the chest. They occur as a result of violent respiration, cough, awkward movements, or during parturition. Secondary factors are pulmonary tuberculosis, pulmonary emphysema or any other pulmonary infection, fragility of the bones from old age, osteoporosis, and diffuse diseases of the bones.

A 62-year-old man was hospitalized in an advanced stage of laryngeal histoplasmosis, pulmonary emphysema, and diffuse osteoporosis. Multiple, bilateral fractures of the posterior surfaces of the 6th, 7th, 8th, and 9th ribs occurred without any symptoms and within an interval of a few days after hospitalization. The fractures were painless, both spontaneously and on palpation, and were detected during a roentgen-ray examination of the chest. Lack of tendency to consolidate was shown both in the roentgenograms and by a biopsy specimen.

Ruptured Abdominal Aortic Aneurysm. J. A. Elliot, A. D. McKenzie and W. B. Chung. Surgery 46:605-617 (Sept.) 1959 [St. Louis].

The authors review observations on 28 patients with ruptured aortic aneurysm, whom they observed from January, 1956, to December, 1958. All the patients had frank ruptures with recent retroperitoneal hemorrhage. Three patients were operated on but died before completion of the procedure; in 4 no surgical therapy was attempted; and in the remaining 21 the aneurysms were resected and replaced by grafts. The majority of the patients on whom resection was performed suffered from serious coincidental disease. Thirteen were in collapse prior to the operation. Nine survived the operation for more than one month. With increase in experience the diagnosis of ruptured aneurysm was made more readily. However, physicians generally seemed to encounter difficulties, since there was considerable delay prior to the diagnosis. Ruptured aneurysm should be added to the differential list of abdominal catastrophes. Immediate operation and aortic control are the most important considerations in treatment; delay invites collapse. Other resuscitative measures have proved to be of incidental importance. The technique of the abdominal operative procedure is described.

Highlights in the experience of these authors were the use of an aortic compressor to obtain proximal control and the piecemeal excision of the aneurysm, with a protective patch left on vulnerable veins. Immediate postoperative complications were impaired leg circulation, oliguria, evisceration, other arteriosclerotic catastrophes, and mechanical obstruction of the small intestine. Two late complications of the replacement procedure were erosion of the proximal anastomosis into the duodenum and fatal gastrointestinal hemorrhage; these occurred at 6 and 33 months respectively. The homograft in the second case showed marked arteriosclerotic degeneration, and this experience as well as the availability of prosthetics, has induced the authors to prefer the latter.

Venous Thromboembolism: A Summary of 10 Years' Experience with 610 Patients and the Evolution of a Routine Management. J. N. Shadid. Surgery 46:588-604 (Sept.) 1959 [St. Louis].

The 3 important interacting factors to consider in thromboembolism are Virchow's triad of vascular damage, slowing of the blood flow, and unknown abnormalities in blood composition. While the amount of vacsular damage and stasis can be clinically estimated, no reliable index of the blood abnormalities was available. In the belief that studies of total physicochemical blood changes might provide an adequate answer, a simple bedside drop test for blood to reflect these changes was devised and applied. The experiences gained with the use of this test on 610 patients with known or suspected venous thromboembolism during the past 10 years indicate that its results, considered in relation to venous damage and blood flow, are trustworthy guides to lead the majority of such patients safely to recovery.

The test consists essentially in timing, under standard conditions of temperature and pressure, the interval taken by 14 drops to fall away from the tip of a standardized and sterilized test instrument containing 1 ml. of blood drawn directly into it from a vein. This drop-measuring instrument (stactometer) is made up of a 1-ml. tuberculin-type syringe barrel with a 25-gauge, ½-in. hypodermic needle attached. The blood drop time thus obtained is divided by the water drop time standard, which has been previously established for each stactometer by timing its delivery of 14 drops from 1 ml. of distilled water at 25 C. The result is the stactometric ratio (SR) and represents the combined effects of viscosity, surface tension, and specific gravity, which are reflections of the physicochemical state of the blood. Since the rate of blood dropping from the stactometer is dependent on the combined effects of the cellular and plasma elements, a hematocrit determination was performed on the same sample of blood. The test drops and the remainder of the milliliter of blood were caught in a heparinized test tube and used to provide the hematocrit figure. The SR and hematocrit of each subject were recorded on a graph. It was found that the SR line was consistently below the hematocrit line when the subject was in a state of well-being and rose above the hematocrit line when he was under mental or physical stress. This empirical relationship between the SR and hematocrit figures made the hematocrit a convenient base line along which SR fluctuations could be plotted in terms of plus or minus variations.

In all of the 610 patients a presumptive diagnosis of venous thrombosis, pulmonary embolism, or both had been made by referring physicians. Sixty of the patients could not be followed with serial determinations. A routine of management of a patient with suspected or obvious venous thromboembolism is presented. The results of this routine of management in 285 patients are recorded and are compared with the earlier results in 265 patients. It was found that the routine management (*a*) helps dispel much of the doubt from uncertain clinical situations associated with venous thromboembolism, (*b*) more definitely outlines the types and duration of treatment and safely minimizes the period of necessary observation to less than 2 weeks in 90% of the patients and indicates the need for anticoagulant therapy in only 60% of the patients, and (*c*) isolates for concentrated attention those patients requiring prolonged, meticulous treatment and those for whom new treatments should be found.

Spontaneous Hemopneumothorax. P. Bourgeois, G. Rollin and P. Dreyfus. Rev. tuberc. 23:513-532 (May-June) 1959 (In French) [Paris].

Hemopneumothorax, which is produced by the appearance, rarely simultaneous, usually successive, of air and blood in the pleural cavity, has been studied by the authors in the light of 2 cases presented in detail and 286 cases found in the literature. Spontaneous hemopneumothorax is infrequent, estimates of its incidence in relation to the total number of cases of spontaneous pneumothorax ranging from 4 to 12%. It occurs chiefly in men; only 11 cases, or about 4%, have been reported in women. More than 80% of the cases observed occurred in young men between the ages of 17 and 32 years (average, 27 years). The history revealed an occupation involving physical work or habitual participation in sports in most cases. The mortality rate has been variously estimated at from 15 to 25%, but this figure is, in fact, excessive, because, although all fatal cases are presumably reported, many mild ones are probably either not diagnosed or not published. Recovery in nonfatal cases usually takes place without sequelae of any kind within 5 to 8 weeks (3 if the condition is minimal).

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PEDIATRICS

Cherubism: Familial Fibrous Dysplasia of the Jaws. N. Thompson. Brit. J. Plast. Surg. 12:89-103 (July) 1959 [Edinburgh].

The author presents the history of a boy with painless, progressive, and disfiguring enlargement of the lower face and jaws. The child showed no abnormalities until he was 2 years old. A photograph taken at the age of 2 years and 5 months showed symmetrical and bilateral swelling of the lower face. This enlargement had continued in gradually progressive fashion throughout the subsequent years. At 5 years of age there was a massive symmetrical enlargement of both maxillae and both sides of the mandible, lending a somewhat pugnacious aspect to the face. The mandible showed on its outer aspect multiple lobulations of 1-to-4-cm. diameter, smooth and ill-defined, bony hard and not tender, and covered intraorally by normal mucosa. Smaller and more discrete lobulations, also smooth and bony hard, were easily palpable on the anterior surface of both maxillae. The alveolus of both jaws was broadened and flattened. The maxillae showed an acutely vaulted, narrow V-shaped, hard palate. The teeth were tilted and in poor occlusion. The submandibular lymph nodes showed bilateral, firm, smooth, nontender, discrete, mobile enlargement of moderate degree.

After describing the roentgenologic aspects and the biopsy specimens taken during the first stage of the operative treatment, the author says that a satisfactory reduction was obtained, but the mandible was inadvertently fractured during the second operation. Great difficulty was encountered in immobilizing the fragments, the often ectopic and deciduous teeth providing an inadequate foundation for splints, and the fibrous nature of the mandible rendering internal fixation impossible. Despite subsequent bone graft, union of the fracture remained fibrous, though function was good. Roentgenography at the age of 8 years revealed that the pathological process continues to progress.

An hereditary factor is involved in this case in that in the boy's maternal grandmother swelling of the lower face had been noticed at the age of 3 to 4 years. This increased steadily throughout her schooldays, but became less noticeable after the age of 20 years. Her condition thereafter steadily improved.

In summarizing previously reported cases of cherubism, the author mentions a report by Jones in 1933 on 3 siblings, aged 6, 5, and 4 years, respectively, who had a bilateral, apparently multilocular cystic disease of both jaws, resulting in marked fulness in the region of the cheeks and jaws, which was enhanced by enlargement of the submandibular lymph nodes. The eyes were described as having "an upward cast," the alveolar ridges were wide, the teeth misplaced or absent. In a subsequent report on this family, when Jones mentioned the peculiar, grotesque, cherubic appearance, he suggested that the term "cherubism" would seem appropriate. Although few subsequent observers have stressed the upturned eyes upon which it was chiefly founded, the pseudonym has persisted.

The boy presented by the author did not have the upturned eyes of cherubism, but a roentgenogram of the chest disclosed peculiar cyst-like changes in the anterior ends of all ribs on both sides. This is the first time involvement of the ribs has been mentioned in this disease. It is assumed that the hereditary element in cherubism arises as a spontaneous mutation of the germ cell. The familial incidence of the disease is the greatest single barrier to explaining cherubism as a fibrous dysplasia of bone, for it does not occur in any other example of the latter. Possibly an inherited predisposition, on which some subsequent factor (traumatic, infective, hormonal) becomes superimposed, may prove an ultimate explanation.

Testosterone-Induced Remission in Aplastic Anemia. N. T. Shahidi and L. K. Diamond. A. M. A. J. Dis. Child. 98:293-302 (Sept.) 1959 [Chicago].

The authors describe a new approach to the therapy of aplastic anemia and the results obtained with it in 5 children, ranging in age from 5 to 15 years; the 1st and 4th patients were male, and the others were female. In addition to corticosteroid therapy and transfusions of platelets, fresh blood, and stored blood as needed, these children were treated with testosterone. The time elapsed between diagnosis and the start of testosterone therapy varied from 6 months to one year in 4 patients, during which they were treated with transfusions and corticosteroids without response. One patient was started on testosterone treatment a few days after the diagnosis was made. Testosterone was used as testosterone propionate or methyltestosterone in the form of 10-mg. buccal Linguets in the dosage of 1 or 2 mg. per kilogram of body weight per day. In addition, one patient was given testosterone enanthate intramuscularly in the dosage of 3 mg. per kilogram of body weight twice weekly. Corticosteroids were administered as triamcinolone, the dosage ranging from 12 to 8 mg. per day.

The bone marrow and peripheral blood studies revealed improvement, beginning with early erythroid regeneration, and beneficial effect of testosterone was also noted on myelopoiesis. Reticulocytosis, with subsequent rise in the hemoglobin level, occurred in all except the 4th child who died. Yet postmortem examination of the bone marrow in the latter patient showed signs of regeneration with erythroid hyperplasia; this was also found in the liver and spleen. Reticulocyte response, however, did not occur shortly after the institution of therapy, as is often seen in patients with other varieties of anemia given specific therapy. The time lapse between the start of treatment and the occurrence of significant reticulocytosis was 1 or 2 months in the 1st, the 3rd, and the 5th child and was 5 months in the 2nd child. The reticulocytosis was accompanied, or succeeded, in all instances by a rise in the hemoglobin level, so that further transfusions were unnecessary.

Continuation of treatment with testosterone and corticosteroids produced steady increase in the hemoglobin value in all the patients, reaching a peak of 14 Gm. per 100 cc. after 6 months of testosterone therapy in the first child and 3 months in the second. The rise of platelet levels varied greatly in each case. Concomitant with the progress of the bone marrow and peripheral blood changes, the patients showed remarkable clinical improvement. Acne, flushing of the skin, and mild hirsutism occurred in all the patients 2 or 3 months after the institution of testosterone therapy. On one occasion mild papilledema accompanied by headache was noted in the second patient, without any other clinical manifestation. No discrepancy between the chronological age and the bone age was noted at any time. Serum calcium and potassium levels showed no alteration in 2 patients.

Granuloma Annulare: A Rarely Recognized Disease of Childhood. F. Koch and H. Jantzen. Monatsschr. Kinderh. 107:364-367 (Aug.) 1959 (In German) [Berlin].

In the course of the last 10 years the authors observed 28 cases of granuloma annulare at the children's clinic of the University in Giessen, Germany. They gained the impression that the disease is becoming more frequent, since 14 of their 28 patients were observed during the last 3 years. They admit that the increase may be only apparent, and that the more frequent diagnosis of the condition may be the result of greater attention to its lesions. In commenting on the terminology, they agree with Dietel, who suggested that the term "granuloma annulare" would be more correct, because the lesions often appear in ring or half-moon groupings. These lesions are most frequent in persons in the first 2 decades, or even the first 15 years, of life; in persons over 40 years of age they are rare.

The onset of granuloma annulare frequently escapes notice, and the lesions are detected accidentally; further search sometimes discloses additional ones. The lesions are whitish, keloid-like, cutaneous nodules, which cause neither pain nor itching. The ring-shaped groupings rarely exceed the size of a silver dollar. Beginning as a pinhead-sized or pea-sized lesion, the infiltration extends peripherally. Later the center sinks down, and here the skin appears atrophic and slightly pigmented. Ulceration does not take place. In addition to the annular foci, there may be disseminated solitary nodules the size of lentils or peas. These, like the annular lesions, are located in the cutis. The epidermis is not involved. The connective tissue in the middle and deeper layers of the corium shows necrobiotic changes.

After a more detailed description of the histopathological aspects of granuloma annulare, the authors discuss the etiology, pointing out that a relationship to rheumatic disorders and a causal connection with tuberculosis have been suggested. The theory that the condition is a specific chronic infectious disease has been largely given up. Although the possible connection with tuberculosis is still being discussed, there is little corroborating evidence for this connection. There are, however, factors that indicate relations to rheumatic disorders, such as the concurrence of granuloma annulare and articular rheumatism, their simultaneous onset after tonsillitis, and the fact that both diseases have the same age distribution. According to some investigators, granuloma annulare belongs to the so-called collagen diseases, which are characterized by allergically induced changes of the collagenous connective tissue. The prognosis of granuloma annulare can be designated as favorable. In view of its tendency to spontaneous cure, the evaluation of therapeutic methods is difficult.

Acute Leukemia with Bone Changes Simulating Calvé-Perthes Disease. E. Mose. Ugesk. laeger 121: 1224-1226 (Aug. 6) 1959 (In Danish) [Copenhagen].

In acute leukemia of children there are often roentgenologically demonstrable changes in the bones. The changes, which are not specific for leukemia, consist of subperiosteal bony neoformation, osteosclerotic processes, and transverse clarifications in the metaphyses back of the epiphysis line, together with destructive changes, most often in the metaphyses, especially in knee and shoulder joints. The pain in joints and extremities in leukemia is ascribed to the processes in the bones. The pain and certain changes in the bones may appear before definite changes in the blood, especially in aleukemic cases. In a boy, aged 2½ years, with acute leukemia, the changes in the bones in the head of the femur, revealed accidentally on roentgenologic examination occasioned by a trauma, resembled the changes in Calvé-Perthes disease and were at the start the only symptoms of the basic disease. In spite of energetic treatment the blood picture could not be normalized, and the boy died 6 months after the onset of the disease. Autopsy showed no necrosis in the head of the femur or bony neoformation other than that normal for the age. The roentgenologic changes were ascribed to the leukemia.

THERAPEUTICS

Metahexamide Jaundice: Report of a Case. B. Mach, R. A. Field and E. B. Taft. New England J. Med. 261:438-440 (Aug. 27) 1959 [Boston].

Severe liver damage developed in a woman, 65 years of age, after having received metahexamide, a sulfonylurea, for control of diabetes mellitus. The patient was admitted to the hospital with the main complaint of jaundice of one day duration. Nausea, vomiting, and constipation were present for 3 weeks, and dark urine for 5 days, before the admission. There were no other complaints. A mild variety of diabetes, which had been discovered 5 years before the admission, was adequately controlled, first with insulin, then with tolbutamide, which was, in turn, replaced by metahexamide. Metahexamide had been administered in daily doses of 150 mg. for 3 months before the admission. The course in the hospital was benign, and the diabetes was well regulated on insulin therapy.

The microscopic examination of the liver tissue obtained on aspiration biopsy revealed marked loss of liver cells, particularly about the portal areas, with condensation of stroma and infiltration with moderate numbers of histiocytes, lymphocytes, and rare plasma cells. There was disarray of the lobular pattern of remaining liver cells and occasional rounded eosinophilic masses. Some cells also exhibited ballooning of their cytoplasm. Intracanalicular bile stasis was present, which was not a prominent feature. Mitotic figures were not seen. Since discharge, the patient has remained asymptomatic, and liver-function tests have approached normal values.

Laboratory and histological findings suggest that the lesion in this patient was mainly hepatocellular and resembled that of a severe viral hepatitis or of iproniazid toxicity. Carbutamide, the first sulfonylurea which was clinically experimented with as a hypoglycemic drug, had to be abandoned after the occurrence of several deaths because of hepatic complications. Both metahexamide and carbutamide contain an amino group on the phenyl ring. It seems that the aminophenyl group contributes a strong hepatocellular toxicity to the sulfonylurea agents.

Chlorpropamide in the Management of Diabetes. S. J. N. Sugar, L. J. Thomas and T. M. Eugenio. A. M. A. Arch. Int. Med. 104:360-364 (Sept.) 1959 [Chicago].

The authors treated 84 patients with diabetes mellitus with chlorpropamide (Diabinese) for periods varying from 2 to 11 months. Of the 84 patients, 37 had been treated previously with insulin or partly controlled with diet, and 47 had received tolbutamide but were not in control. Of the latter group, 10 had failed to respond to tolbutamide within the first month of treatment (primary tolbutamide failures), and 37 had slipped out of control after a variable period of satisfactory management with tolbutamide (secondary tolbutamide failures). A dose of 0.5 Gm. of chlorpropamide per day was selected as starting therapy. After one week, if control was not satisfactory, the dose was increased by increments of 0.25 Gm. Most patients responded to a daily dose of 0.25 to 0.5 Gm. No patients benefited by an increase in the dose to more than 1.5 Gm. Twenty-seven (73%) of the 37 patients previously treated with insulin were adequately managed with chlorpropamide alone. Only 2 of the 10 primary tolbutamide failures responded to chlorpropamide. Twenty-three (62%) of the 37 secondary tolbutamide failures responded to chlorpropamide. Best results were noted in patients over 40 years of age with known duration of diabetes mellitus of less than 10 years, requiring less than 40 units of insulin per day.

Toxicity to chlorpropamide was somewhat related to dosage. Doses of more than 1 Gm. per day were frequently associated with unpleasant side-effects. Gastrointestinal symptoms, chest pain, and muscular weakness were the most prominent side-effects. Occasionally these were relieved by reduction in the dose of the drug. Chlorpropamide is more potent than tolbutamide in blood-sugar-lowering ability. Unstable diabetics of any age are poor candidates for control with chlorpropamide.

Chlorpropamide Therapy of Diabetes: An Appraisal. R. C. Stewart, E. U. Piazza, H. Hyman III and D. Hurwitz. New England J. Med. 261:427-430 (Aug. 27) 1959 [Boston].

Chlorpropamide was administered orally for 3 months to 56 outpatients with diabetes mellitus. The initial daily dosage of 1 Gm. of chlorpropamide produced hypoglycemia and side-effects in several patients. These symptoms were less frequent when the daily dose level was subsequently decreased to 500 mg. Six patients were eliminated because they were lost to follow-up study. The drug had to be withdrawn in 12 patients—in 8 because of poor control and in 4 because of severe side-effects. These side-effects were excessive salivation, nausea, and anorexia in one, jaundice (obstructive type) in one, generalized erythema multiforme accompanied by fever and eosinophilia in one, and vertigo and fatigue in one. The only laboratory test that showed abnormality during the study was the alkaline phosphatase.

Of 38 patients who completed the therapy, excellent results were obtained in 19, good in 8, fair in 8, and poor in 3. The duration of diabetes was less than 10 years in 36 patients and more than 10 years in 14. Diabetes of less than 10 years' duration was adequately controlled with chlorpropamide in 23 patients (64%), whereas in instances of more than

10 years' duration it was adequately controlled in 7 (50%). Twenty-seven patients had previously received tolbutamide. Three patients had better control on tolbutamide, and 16 on chlorpropamide; 8 had the same control on either drug. The more prolonged action of chlorpropamide was an advantage over tolbutamide.

Thirty-four patients who had previously taken insulin were suddenly withdrawn from insulin and transferred to the amount of chlorpropamide necessary for maximal control. Thirteen patients had better control on chlorpropamide, and 13 on insulin; 8 had the same control on either drug. Although more patients had adequate control on insulin than on chlorpropamide, excellent control was obtained in more patients (13) who received chlorpropamide than in those (4) who received insulin. This comparison suggests that chlorpropamide, when effective, may provide more prolonged and constant control than intermediate-acting insulin. This study is based on short-term observations.

Mannomustine in Treatment of Leukemias, Polycythemia, and Malignant Disorders. A. M. Barlow, J. T. Leeming and J. F. Wilkinson. Brit. M. J. 2:208-213 (Aug. 22) 1959 [London].

A new cytostatic compound, mannomustine, has been used in the treatment of 45 patients with leukemias, polycythemia, reticulosis, and malignant disease. Since the administration of doses as high as 200 to 500 mg. of mannomustine in one injection proved to produce frequent and severe toxic reactions, the maximal single dose was restricted to 100 mg. daily or on alternate days, and this was found to be the most satisfactory dosage scheme. The required total dosage varied from patient to patient and with the particular disease.

In only 2 of 12 patients with myeloid leukemia was a favorable response to mannomustine therapy observed; however, both patients relapsed shortly. In the remaining 10 patients control was inadequate and of short duration. The responses to further courses of mannomustine given to 6 patients were even less satisfactory than those after the initial courses. A considerable variation in response could be seen in 3 patients with chronic lymphocytic leukemia. Mannomustine therapy proved to be of some value in the treatment of 6 patients with acute leukemia, in whom the initial white blood cell counts were high. The total white blood cell count was reduced to relatively normal levels, facilitating the subsequent action of prednisolone and blood transfusions. In none of these patients was complete remission obtained.

Mannomustine appears to be of some value in the treatment of reticulosis, follicular lymphoreticulosis, reticulosarcoma, multiple myeloma, and polycythemia. In 5 of 14 patients with reticulosis, good responses were observed, while they were moderately good in 4. However, the responses were not as good as those achieved with tri(2-chloroethyl)-amine hydrochloride (Trillekamin); many more injections were required with mannomustine, and these injections produced more toxic effects, generally and on the bone marrow, than those obtained with Trillekamin. Mannomustine would appear to be more effective than triethylenethiophosphoramide (Thio-Tepa) in patients with reticulosis, as complete regressions of hepatomegaly, splenomegaly, and mediastinal lymphadenopathy have been obtained in most cases in this series, whereas Thio-Tepa has been relatively inactive in reticulosis involving these structures. Two patients with follicular lymphoreticulosis and one with reticulosarcoma benefited from treatment, and one patient with multiple myeloma showed such good symptomatic and objective improvement that further treatment with mannomustine, alone or in combination with urethane, was advisable. Mannomustine was of little value in 5 patients with carcinoma. In 2 of these patients severe anemia and thrombocytopenia developed, which may well have contributed in some degree to their more rapid deterioration. Satisfactory remissions were obtained in 4 patients with polycythemia.

Toxic effects of mannomustine therapy can be severe, particularly on the bone marrow and especially if a second course has been given within 4 months. Gastrointestinal side-effects, nausea, or vomiting occurred in 42% of the patients after single doses of 1.5 to 2 mg. per kilogram; as high as 70% were affected after doses of 3 to 7 mg. per kilogram.

The Present Status of the Clinical Evaluation of Fibrinolysin. R. V. Chapple and H. O. Singher. Canad. M. A. J. 81:231-234 (Aug. 15) 1959 [Toronto].

The authors report on 322 patients with thromboembolic disease, who were treated with a preparation of human fibrinolysin in some of the larger hospitals in Boston, New York, Washington, and Philadelphia. Alteration in the coagulation mechanism or hemorrhagic complications did not occur in any of the patients. The concomitant use of anticoagulants, either heparin or one of the coumarin types, did not produce any deleterious effects. Doses between 50,000 and 100,000 units of fibrinolysin were significantly more effective than doses below 50,000 units. Fibrin clots are usually well organized within 5 to 7 days after their formation. This organization retards the lytic action of fibrinolysin. In view of this limitation of lytic activity, the maximum therapeutic response in patients with phlebothrombosis was obtained in recently formed clots. Excellent results with a return of limb measurement to normal within 48 to 72 hours were obtained in 57 (83%) of 69 patients with phlebothrom-

THERAPEUTICS

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The microscopic examination of the liver tissue obtained on aspiration biopsy revealed marked loss of liver cells, particularly about the portal areas, with condensation of stroma and infiltration with moderate numbers of histiocytes, lymphocytes, and rare plasma cells. There was disarray of the lobular pattern of remaining liver cells and occasional rounded eosinophilic masses. Some cells also exhibited ballooning of their cytoplasm. Intracanalicular bile stasis was present, which was not a prominent feature. Mitotic figures were not seen. Since discharge, the patient has remained asymptomatic, and liver-function tests have approached normal values.

Laboratory and histological findings suggest that the lesion in this patient was mainly hepatocellular and resembled that of a severe viral hepatitis or of iproniazid toxicity. Carbutamide, the first sulfonylurea which was clinically experimented with as a hypoglycemic drug, had to be abandoned after the occurrence of several deaths because of hepatic complications. Both metahexamide and carbutamide contain an amino group on the phenyl ring. It seems that the aminophenyl group contributes a strong hepatocellular toxicity to the sulfonylurea agents.

Chlorpropamide in the Management of Diabetes. S. J. N. Sugar, L. J. Thomas and T. M. Eugenio. A. M. A. Arch. Int. Med. 104:360-364 (Sept.) 1959 [Chicago].

The authors treated 84 patients with diabetes mellitus with chlorpropamide (Diabinese) for periods varying from 2 to 11 months. Of the 84 patients, 37 had been treated previously with insulin or partly controlled with diet, and 47 had received tolbutamide but were not in control. Of the latter group, 10 had failed to respond to tolbutamide within the first month of treatment (primary tolbutamide failures), and 37 had slipped out of control after a variable period of satisfactory management with tolbutamide (secondary tolbutamide failures). A dose of 0.5 Gm. of chlorpropamide per day was selected as starting therapy. After one week, if control was not satisfactory, the dose was increased by increments of 0.25 Gm. Most patients responded to a daily dose of 0.25 to 0.5 Gm. No patients benefited by an increase in the dose to more than 1.5 Gm. Twenty-seven (73%) of the 37 patients previously treated with insulin were adequately managed with chlorpropamide alone. Only 2 of the 10 primary tolbutamide failures responded to chlorpropamide. Twenty-three (62%) of the 37 secondary tolbutamide failures responded to chlorpropamide. Best results were noted in patients over 40 years of age with known duration of diabetes mellitus of less than 10 years, requiring less than 40 units of insulin per day.

Toxicity to chlorpropamide was somewhat related to dosage. Doses of more than 1 Gm. per day were frequently associated with unpleasant side-effects. Gastrointestinal symptoms, chest pain, and muscular weakness were the most prominent side-effects. Occasionally these were relieved by reduction in the dose of the drug. Chlorpropamide is more potent than tolbutamide in blood-sugar-lowering ability. Unstable diabetics of any age are poor candidates for control with chlorpropamide.

Chlorpropamide Therapy of Diabetes: An Appraisal. R. C. Stewart, E. U. Piazza, H. Hyman III and D. Hurwitz. New England J. Med. 261:427-430 (Aug. 27) 1959 [Boston].

Chlorpropamide was administered orally for 3 months to 56 outpatients with diabetes mellitus. The initial daily dosage of 1 Gm. of chlorpropamide produced hypoglycemia and side-effects in several patients. These symptoms were less frequent when the daily dose level was subsequently decreased to 500 mg. Six patients were eliminated because they were lost to follow-up study. The drug had to be withdrawn in 12 patients—in 8 because of poor control and in 4 because of severe side-effects. These side-effects were excessive salivation, nausea, and anorexia in one, jaundice (obstructive type) in one, generalized erythema multiforme accompanied by fever and eosinophilia in one, and vertigo and fatigue in one. The only laboratory test that showed abnormality during the study was the alkaline phosphatase.

Of 38 patients who completed the therapy, excellent results were obtained in 19, good in 8, fair in 8, and poor in 3. The duration of diabetes was less than 10 years in 36 patients and more than 10 years in 14. Diabetes of less than 10 years' duration was adequately controlled with chlorpropamide in 23 patients (64%), whereas in instances of more than

10 years' duration it was adequately controlled in 7 (50%). Twenty-seven patients had previously received tolbutamide. Three patients had better control on tolbutamide, and 16 on chlorpropamide; 8 had the same control on either drug. The more prolonged action of chlorpropamide was an advantage over tolbutamide.

Thirty-four patients who had previously taken insulin were suddenly withdrawn from insulin and transferred to the amount of chlorpropamide necessary for maximal control. Thirteen patients had better control on chlorpropamide, and 13 on insulin; 8 had the same control on either drug. Although more patients had adequate control on insulin than on chlorpropamide, excellent control was obtained in more patients (13) who received chlorpropamide than in those (4) who received insulin. This comparison suggests that chlorpropamide, when effective, may provide more prolonged and constant control than intermediate-acting insulin. This study is based on short-term observations.

Mannomustine in Treatment of Leukemias, Polycythemia, and Malignant Disorders. A. M. Barlow, J. T. Leeming and J. F. Wilkinson. Brit. M. J. 2:208-213 (Aug. 22) 1959 [London].

A new cytostatic compound, mannomustine, has been used in the treatment of 45 patients with leukemias, polycythemia, reticulosis, and malignant disease. Since the administration of doses as high as 200 to 500 mg. of mannomustine in one injection proved to produce frequent and severe toxic reactions, the maximal single dose was restricted to 100 mg. daily or on alternate days, and this was found to be the most satisfactory dosage scheme. The required total dosage varied from patient to patient and with the particular disease.

In only 2 of 12 patients with myeloid leukemia was a favorable response to mannomustine therapy observed; however, both patients relapsed shortly. In the remaining 10 patients control was inadequate and of short duration. The responses to further courses of mannomustine given to 6 patients were even less satisfactory than those after the initial courses. A considerable variation in response could be seen in 3 patients with chronic lymphocytic leukemia. Mannomustine therapy proved to be of some value in the treatment of 6 patients with acute leukemia, in whom the initial white blood cell counts were high. The total white blood cell count was reduced to relatively normal levels, facilitating the subsequent action of prednisolone and blood transfusions. In none of these patients was complete remission obtained.

Mannomustine appears to be of some value in the treatment of reticulosis, follicular lymphoreticulosis, reticulosarcoma, multiple myeloma, and polycythemia. In 5 of 14 patients with reticulosis, good responses were observed, while they were moderately good in 4. However, the responses were not as good as those achieved with tri(2-chloroethyl)-amine hydrochloride (Trillekamin); many more injections were required with mannomustine, and these injections produced more toxic effects, generally and on the bone marrow, than those obtained with Trillekamin. Mannomustine would appear to be more effective than triethylenethiophosphoramide (Thio-Tepa) in patients with reticulosis, as complete regressions of hepatomegaly, splenomegaly, and mediastinal lymphadenopathy have been obtained in most cases in this series, whereas Thio-Tepa has been relatively inactive in reticulosis involving these structures. Two patients with follicular lymphoreticulosis and one with reticulosarcoma benefited from treatment, and one patient with multiple myeloma showed such good symptomatic and objective improvement that further treatment with mannomustine, alone or in combination with urethane, was advisable. Mannomustine was of little value in 5 patients with carcinoma. In 2 of these patients severe anemia and thrombocytopenia developed, which may well have contributed in some degree to their more rapid deterioration. Satisfactory remissions were obtained in 4 patients with polycythemia.

Toxic effects of mannomustine therapy can be severe, particularly on the bone marrow and especially if a second course has been given within 4 months. Gastrointestinal side-effects, nausea, or vomiting occurred in 42% of the patients after single doses of 1.5 to 2 mg. per kilogram; as high as 70% were affected after doses of 3 to 7 mg. per kilogram.

The Present Status of the Clinical Evaluation of Fibrinolysin. R. V. Chapple and H. O. Singher. Canad. M. A. J. 81:231-234 (Aug. 15) 1959 [Toronto].

The authors report on 322 patients with thromboembolic disease, who were treated with a preparation of human fibrinolysin in some of the larger hospitals in Boston, New York, Washington, and Philadelphia. Alteration in the coagulation mechanism or hemorrhagic complications did not occur in any of the patients. The concomitant use of anticoagulants, either heparin or one of the coumarin types, did not produce any deleterious effects. Doses between 50,000 and 100,000 units of fibrinolysin were significantly more effective than doses below 50,000 units. Fibrin clots are usually well organized within 5 to 7 days after their formation. This organization retards the lytic action of fibrinolysin. In view of this limitation of lytic activity, the maximum therapeutic response in patients with phlebothrombosis was obtained in recently formed clots. Excellent results with a return of limb measurement to normal within 48 to 72 hours were obtained in 57 (83%) of 69 patients with phlebothrombosis, who were treated with fibrinolysin within 3 to 5 days after clot formation. Of 63 patients treated with fibrinolysin when their clots had been present for more than 5 days, an excellent response was obtained in only 39 (62%).

Pulmonary embolism is primarily based on the fragmentation of an existing thrombus. Pulmonary embolism appeared concomitantly in 3 of 172 patients on fibrinolysin therapy for phlebothrombosis. With the maintenance of an adequate systemic fibrinolytic level, no sequelae occurred. This incidence of pulmonary embolism was possibly less than the usual occurrence of pulmonary emboli. The only major side-reaction observed with fibrinolysin therapy was a temperature response varying from mild (below 102 F [38.5 C]) to severe (over 102 F). Only 29% of the 322 patients fell into this latter category. An urticarial type of reaction occurred in less than 1% of the patients. Some nausea and/or vomiting occurred in those patients with an exceedingly high temperature response.

At present fibrinolysin appears very promising in patients with thromboembolic disease. Fibrinolysin must not be considered as an anticoagulant. It is a lytic agent and will immediately lyse a forming clot owing to its affinity for fibrin. It proved therapeutically effective in patients with phlebothrombosis, thrombophlebitis, and pulmonary embolism when used appropriately. It is apparent that fibrinolysin, as now produced and used in a dosage ranging from 25,000 to 250,000 units, is therapeutically acceptable from a clinical pharmacological viewpoint. Large-scale statistical studies will alone determine its effectiveness in some of the many therapeutic indications. There has been no significant relation between the potency of fibrinolysin and the presence or absence of concomitant anticoagulant therapy. It is, however, important to consider ambulatory anticoagulant therapy after fibrinolysin administration to prevent the formation of further thrombi. While the offending thrombus is lysed, the associated intimal damage usually requires a longer period for complete epithelization.

RADIOLOGY

Contribution to the Roentgen-ray Picture of Pulmonary Aspergillosis. H. Voigt and A. Krebs. Beitr. Klin. Tuberk. 120:331-340 (no. 5) 1959 (In German) [Berlin].

The authors report the roentgenologic findings in 2 men, aged 27 and 40 years, a 22-year-old woman, a 14-year-old girl, and a 16-year-old boy, who underwent lobectomy or segmental pulmonary resection for cavitary disease of the upper lobe associated with repeated hemoptysis. Bacteriological-mycological examination of the surgical specimens revealed the presence of Aspergillus fumigatus in all 5 patients. The chest roentgenograms and particularly the tomograms of the 27-year-old man and of the girl showed the characteristic shadow of aspergillosis, i. e., a rounded density with a radiolucent cap. The chest roentgenograms of the other 3 patients were not characteristic. In the 40-year-old man, the fungus had settled in a cavity of questionable origin, and the tomogram showed a cavity with mirror formation and a dilated draining bronchus. The tomogram of the boy showed a cavity with calcium deposits. The roentgenogram and the tomogram of the woman showed a shadow the size of a palm in the cardiac-diaphragmatic angle which decreased in density upward. In the last 2 patients, examination of the surgical specimen revealed A. fumigatus in bronchiectatic cavities which no longer showed a communication with the bronchial tree. The authors believe that, even in the presence of uncharacteristic roentgenologic findings, the uniform clinical symptomatology, particularly hemoptysis, and the repeated occurrence of bronchitis or bronchopneumonia in the absence of Mycobacterium tuberculosis should be considered suggestive of a fungus disease of the lung, particularly in young patients.

PUBLIC HEALTH

Paralytic Poliomyelitis Trends, Canada, 1958. D. Kubryk. Canad. M. A. J. 81:228-231 (Aug. 15) 1959 [Toronto].

In 1958, for the first time in 6 years since the advent of the Salk vaccine, reported cases of paralytic poliomyelitis in Canada increased sharply under the impact of an epidemic in the province of Manitoba that accounted for 107 (42%) of the total of 253 cases, and a lesser outbreak in the province of Quebec with 79 cases, accounting for 31% of the total number. The number of paralytic cases of poliomyelitis was 43% higher than in 1957. Most of these cases occurred among unvaccinated persons, and in the province of Quebec particularly among children of preschool age. It seems that the adult population of the province of Quebec possesses a higher degree of naturally acquired immunity than that of the other provinces in which the number of adults and of preschool children involved in the epidemic was about the same. In the preschool age group the highest attack rates were between the ages of 1 and 3 years, the peak having shifted from the 2-year-olds in 1957 to the 1-year-olds in 1958. The attack rate in the 1-year-olds and those aged less than 1 year was about 3 times higher in 1958 than in 1957. The efficacy of vaccination was proved again. Most of the patients who stated that they had been vaccinated had in reality received only 1 or 2 injections. Twenty-nine deaths occurred among the 253 patients, a mortality rate of 11.4% as compared with that of 14.7% in 1957. Most of these deaths occurred among adults.

If the repetition of the 1958 outbreak is to be avoided, it is imperative that the drive for vaccination receive the fullest kind of backing. Now that the school age group is fairly well protected, the same protection should be extended to the preschool age group, in which most of the cases occur, and to adults, in whom most of the deaths have occurred. Among the adults, the 25-34 age group should receive special attention; these are the young parents who may be infected by their vaccinated children acting as symptomless carriers.

A Comparison of the Responses of 100 Infants to Primary Poliomyelitis Immunization with Two and with Three Doses of Vaccine. F. T. Perkins, R. Yetts and W. Gaisford. Brit. M. J. 1:1083-1086 (April 25) 1959 [London].

Previous investigations revealed that in only a small proportion of infants, under the age of 10 weeks, could a satisfactory basal immunity be established by the injection of 2 doses of poliomyelitis vaccine. This prompted the authors to study the response to 2 and 3 doses of the vaccine in 45 1-week-old infants and in 55 16-week-old infants. Of the 45 1-week-old infants, 36 received 3 doses, and 9 received only 1 dose. The vaccine was given at intervals of 4 weeks, and all infants were 1 week old at the time they received the first shot. Each dose contained 2 ml. of the vaccine and was given by injecting 1 ml. into each buttock. The total volume was thus 4 ml. for those who received 2 doses and 6 ml. for those who received 3. All the 55 16-week-old infants were given 3 doses of vaccine intramuscularly, each of 1 ml. spaced at intervals of 4 weeks. All were 15 to 17 weeks of age at the time they received the first dose.

It is evident from the results with the 1-week-old infants that the responses to 2 doses, each of 2 ml., were no better than the responses obtained previously in a similar group of infants who were given 2 doses, each of 1 ml. The response to 3 doses, 2 ml. each, was somewhat better, but there was a high proportion of nonresponders to all 3 types. The responses to 2 doses of the vaccine, 1 ml. each, in the 16-week-old infants who had little or no maternal antibody were no better than those obtained in a previous study with 10-week-old infants on a similar schedule. Three doses, however, gave a decided improvement; 83% of the infants responded to type 1, and all the infants responded to types 2 and 3.

The geometric mean antibody titers reflected the greater immunizing power of the 3-dose schedule. Although a high proportion of infants with no maternal antibody responded to immunization, less satisfactory results were obtained with those who had maternal antibody. After 2 doses, only 11% responded to type 1, 39% to type 2, and 52% to type 3, and after 3 doses the corresponding figures were 36, 62, and 91%. It is thus evident that the 3-dose schedule was unable in all cases to overcome the maternal antibody interference, especially with type 1. In order to obtain satisfactory immunization to all types in all infants, it is suggested that immunization should be delayed until 6 to 9 months of age, at which time 3 doses of vaccine should be considered as a course of primary immunization.

Results of a Study of the Reactogenic and Immunogenic Properties of Live Anti-Poliomyelitis Vaccine. A. A. Smorodintsev, E. F. Davidenkova, A. I. Drobyshevskaya and others. Bull. World Health Organ. 20:1053-1074 (no. 6) 1959 (In English) [Geneva].

The authors studied the reactogenic and immunogenic properties of live poliomyelitis vaccine made in Leningrad from Sabin strains of low pathogenicity for monkeys. More than 20,000 children of preschool age (6 months to 3 years) and of school age (7 to 14 years) were each given 100,000 tissue-culture infective doses of virus of types 1, 2, and 3, injected either in 3 stages at monthly intervals in the form of monovaccines, or in 2 stages, a monovaccine of type 1 being followed after a month's interval by injection of a divalent vaccine of types 2 and 3. The vaccination caused no symptoms of lesions of the central nervous system or other organs. In the blood of the inoculated children there was a regular build-up of virus-neutralizing antibodies to the serotypes mentioned, the intensity of which depended on the antibody level before vaccination and was in a constant relationship to the multiplication of the virus in the intestinal canal. The antibody titer was maintained at high levels for 6 to 9 months after immunization and fell a little after 12 to 18 months. The vaccinal virus is easily transferred from vaccinated children to contact groups, which are gradually vaccinated by this natural means.

Lengthy and numerous passages of vaccinal strains through the intestinal canal of normal, susceptible children showed that strains may periodically appear which have a higher neurotropic activity for monkeys. This activity, however, did not increase in subsequent passage and returned to the initial level. Results of this study show the harmlessness and high level of immunogenicity of Sabin's live vaccine for the groups of children most susceptible to poliomyelitis and provide a basis for the further study of this important method in larger-scale epidemiologic experiments.

BOOK REVIEWS

Hernia. By Sir Heneage Ogilvie, K.B.E., M. A., M.Ch. Cloth. $6.50. Pp. 135, with 51 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41-43 Maddox St., London, W. 1, England, 1959.

There is a place in the extensive literature on hernia for a thin volume containing the distillate of a mature surgeon's thoughts on this important subject. In a field where types of operations are as numerous as surgeons performing them, a dogmatic approach based on more than three decades of experience and careful observation is welcome. Many surgeons, especially in America, will take issue with some of the author's views, but there are few who will disagree with his insistence on strict adherence to the traditional principles of hernia repair.

The book is well written, and the information is presented in a clear manner. The first chapter concerns the place of apparatus in the treatment of hernia. The second chapter, the best section in the volume, deals with the general principles in the operative repair of hernia and presents many personal views. These are the result of the author's experiences with a variety of techniques and materials. They are his opinions, he states them frankly, and he justifies them. He does not hedge, and, to use his own word, he is not obsequious. He prefers small catgut but comments on various other suture materials. He talks of needles, describes silver wire filigree, remarks on sheets of fascia, derma, and nylon, and ends with a note on tantalum. In succeeding chapters he refers to points made earlier and amplifies them. Fascial strips as introduced by Gallie and le Mesurier are considered unsuitable for the repair of inguinal hernias.

A discussion of inguinal hernia occupies the major part of the space in this book, as it should. The anatomy and function of the various structures in the inguinal region are presented as this surgeon sees them in the living subject. The author then discusses the forces and changes leading to the development of inguinal hernia and proceeds to the general principles of operations on the inguinal canal. Local anesthesia is favored in many instances and is described more fully than in most textbooks. The author's standard operations for three degrees of increasing pathological change found in inguinal hernias are well described and are the rational repair methods adopted after long experience. The management of interstitial, congenital direct, sliding, large, and recurrent hernias; the problem of the undescended testis; and operations for inguinal hernia in infants are described. The chapter on standard operations that are not recommended for inguinal hernias makes interesting reading. Specifically, the author does not like Bassini's operation, Gallie's fascial repair, the McVay principle, Halsted's anterior reconstruction, and others; he gives reasons for his stand. The reader may not concur with all the author's ideas, but he is forced to think again about operations he may have been performing without question.

The presentations on femoral, umbilical, epigastric, incisional, and the rarer spigelian and pelvic hernias are excellent and include first-rate simple illustrations which would in themselves make this small volume worthwhile. Books of this sort are not common. One is usually offered the gamut of operations with no comment as to why the author would use some and not others. The author, from a lifetime of experience, flatly states his views on hernias, which are a subject of continued concern to the active general surgeon. This small personal volume should be a welcome addition to the latter's collection as well as to the libraries of all institutions engaged in the training of surgeons.

Mycoses of Man and Animals. By R. Vanbreuseghem, M.D., Professeur de Parasitologie tropicale à l'Université libre de Bruxelles. Authorized English translation by J. Wilkinson, Ph.D., F.L.S. Cloth. $10.50. Pp. 235, with 48 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Sir Isaac Pitman & Sons, Ltd., Pitman House, Parker St., Kingsway, London, W. C. 2, England, 1958.

Dermatologists and medical and veterinary mycologists should welcome this textbook, which is an English translation of the third part of Dr. Maurice Langeron's admirable "Précis de Mycologie." The book hardly provides material for adverse criticism. The author has expressed his modesty in the following quotation from Terrence: "Since that which you wish cannot happen, you should desire what can happen." Indeed, more is offered in this volume than the modesty expressed in this motto would lead one to anticipate. The book presents a profound study of the common superficial and systemic mycoses, arranged in alphabetical order. A particular feature is that each disease is introduced by a brief review of outstanding historical facts. There follows a discussion of pertinent mycological, clinical, immunological, experimental, and therapeutic data, presented in a clear and concise style. The chapter dealing with dermatophytes raises several controversial issues in relation to classification, but this should not diminish the textbook's real value. The book was apparently in print before the introduction of nystatin, amphotericin B, and griseofulvin, as no mention is made of these important therapeutic advances. More illustrations and a better index would be desirable. The bibliography is adequate. This English translation should receive the same enthusiastic reception as the original French edition.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

HYPERIMMUNE VACCINAL GAMMA GLOBULIN

To the Editor:—*A recent newspaper story told of a rare serum that was rushed from Colorado to Maine to aid in the care of a boy afflicted with eczema vaccinatum. What are the disease and treatment referred to?* M.D., South Carolina.

Answer.—Eczema vaccinatum is an occasional complication of smallpox vaccination. The child who is a likely candidate for the illness has usually not been vaccinated, because of a skin condition, and is exposed to the vaccine through a vaccinated sibling. Eczema vaccinatum in children 4 years of age or less is a life-threatening disease because of the massive nature of virus involvement. In addition to the spread of the infection from the initial contact site to all other eczematous skin areas, including those which may have minimal involvement with eczema, viremia frequently is a complication, as evidenced by the lesions that occur on normal skin. Serologic studies indicate that these patients have a delay in antibody production, and, for many of them, this delay is for the vaccinia virus only. This may be due to the relative immaturity of the patient, or it may denote the overwhelming nature of the antigenic stimulation and mean that any neutralizing antibodies produced are quickly tied up by the virus present and cannot be measured.

Although the total gamma globulin levels may be high in children suffering from eczema, antibody levels to vaccinia virus, during and after a serious infection with vaccinia contracted by accident, may be surprisingly low. No controlled experiments are available because of the serious nature of the disease. It is this consultant's opinion that the administration of hyperimmune vaccinal gamma globulin obtained from recently vaccinated young adults decreases toxemia, limits the spread of the virus, and influences the course favorably. The dose is 0.3 to 0.5 cc. per kilogram of body weight given once intramuscularly, but it may be repeated if the patient does not improve in 24 hours. The material is available through the American Red Cross and from the University of Colorado Medical Center, Denver. Hyperimmune vaccinal gamma globulin has been successfully used in the treatment of a child with generalized vaccinia (without eczema) and vaccinia necrosum (progressive vaccinia). The latter is characterized by complete immunological paralysis and steady progression of virus infection leading to death, unless massive amounts of antibodies and other emergency measures are provided.

Hyperimmune vaccinal gamma globulin will soon be licensed and removed from the experimental designation it now carries. Experience with its use in serious complications of smallpox vaccination is such that its administration as a therapeutic or prophylactic agent should be further evaluated.

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EMOTIONAL ILLNESS

To the Editor:—*A 29-year-old farmer, who has not had previous emotional difficulties, complains of excessive concern about his crops, his financial status, and other problems. Because of this he is unable to do his work. Examination revealed severe depression, intermittent hypertension, with blood pressures up to 160/96 mm. Hg, a protein-bound iodine level of 2.6 mcg. per 100 ml., and a urinary 17-ketosteroid excretion of 36 mg. per day. A repeated measurement of the 17-ketosteroid excretion, after all medication was stopped, was 29 mg. per day. ACTH was given for three days. The 17-ketosteroid excretion was 39 mg. on the second day and 42 mg. on the third. The patient went to another hospital two weeks later and at this time seemed much improved. His attending physician was not impressed by the emotional aspect of his difficulties. He returned home and the depression recurred. Psychiatric consultation was obtained and the patient had an excellent response to shock therapy. What is the management of this patient from this point on?*

Clarence E. Hicks, M.D., Hereford, Texas.

Answer.—Before deciding which course to pursue, one must appraise the patient's symptoms and the laboratory findings. The clinical findings are those of an acute emotional depression in a young man, and there is evidence of autonomic imbalance with endocrine involvement. It is significant that the depression disappeared when the patient left home but recurred on his return. The depression was relieved after convulsive shock therapy. It is assumed, since no statement is made about the

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

laboratory findings after electric shock therapy, that they were normal. This may be a simple depression or the depression may be a symptom of a basic incipient schizophrenic psychosis. It is not uncommon to find electrolytic, hormonal, and metabolic disturbances in either case, since emotional stress is known to cause changes in adrenal and thyroid gland activity, the excretion of epinephrine and arterenol, and the excretion of electrolytes. The patient's condition needs further study, with emphasis on psychiatric evaluation and treatment rather than biochemical tests.

TIME OF SERVING MAIN MEAL

To the Editor:—*The amount of fat in the blood is known to increase after a meal and to reach a maximum six hours later. This nutritional lipemia or hyperlipemia increases the blood coagulability, and, since rest and not physical stress predisposes to coronary and cerebral thrombotic accidents, would it be wiser to have the main (richer in fat) meal at noon than in the evening?*

Herman Schauder, M.D., New York.

Answer.—There is no simple answer to this question, since many factors are involved. That hyperlipemia increases coagulability is questionable. Several observers report no change in coagulability after meals high in fat content and an equal number have found an increased tendency for clot formation. None of the present tests of coagulation is perfect. While rest and stasis may predispose to thrombosis formation, physical activity performed just after a meal may be dangerous for the person with narrowed coronary arteries. Patients frequently relate that anginal pain is most easily brought on by walking after meals. Shifting the main meal to lunch time would accomplish little, unless the custom of a siesta after lunch were to be instituted at the same time. It would seem best to reduce the saturated (animal) fat portion of the meals for persons who have elevated serum lipid levels.

MANAGEMENT OF ADYNAMIC ILEUS

To the Editor:—*What drug can be used to treat a patient with adynamic ileus? What is the effect of d-pantothenyl alcohol (Ilopan) in postoperative ileus?*

Lloyd H. Murdock, M.D., Zwolle, La.

Answer.—Reflex ileus occurring postoperatively may be due to the cumulative effects of anesthesia, surgical trauma, and narcotics. Morphine, methscopolamine, or hexamethonium in repeated large doses can produce ileus. Management includes nasogastric intubation, use of the rectal tube, cholinergic medication (neostigmine or lethanechol), restoration of fluid balance, chemotherapy, and general supportive measures. The preliminary reports on d-pantothenyl alcohol are favorable, but further experience with this drug is warranted. The pantothenic acid component is part of coenzyme A which is essential to the acetylation of choline. Acetylcholine, the physiological transmitter of nerve impulses at various levels of the autonomic nervous system, is required for normal peristaltic intestinal activity. There is little risk of overproduction of acetylcholine by excessive administration of d-pantothenyl alcohol, since the tissue will produce only the amount of acetylcholine it needs and thus excessive cholinergic reactions will be avoided. In fact, the concomitant administration of d-pantothenyl alcohol with cholinesterase inhibitors (such as neostigmine) is contraindicated.

TREATMENT OF SNAKE BITE

To the Editor:—*In* The Journal, *Feb. 14, page 782, it was stated that the coral snake antivenin from Florida is made from cobra venom. There is, in central Florida, a source of true coral snake antivenin which is made in South America and available at the following hospitals in Florida: Morrell Memorial Hospital, Lakeland; Winter Haven Hospital, Winter Haven; Jackson Memorial Hospital, Dade City; and South Florida Baptist Hospital, Plant City.*

The gathering of this information was done by Mr. R. E. Lewis, manager of the Lakeland Surgical Supply, Incorporated.

Although it is true that coral snake bites are not a major problem in Florida, the information is worth passing on to your readers.

F. Layton Bergquist, M.D.
119 Allamanda Dr.
Lakeland, Fla.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*I was not aware of the availability in central Florida of true coral snake antivenin until I too received a letter from Mr. R. E. Lewis. The information is correct. The availability of true coral snake antivenin is not widely known in Florida and even less well-known outside Florida. This information should be of interest to physicians in the southwest, where the Sonoran coral snake (Micrurus euryxanthus) threat is similar to that of the Eastern coral snake (Micrurus fulvius, harlequin snake) in Florida. Although it has been repeatedly stated that coral snake bites in the human are not a major problem (in Florida or elsewhere), to the person who has been bitten by a coral snake it is a major problem indeed.*

SUBJECT INDEX

The letters used to explain in which department the matter indexed appears are as follows: "E," Editorial; "C," Correspondence; "ab," abstracts; the asterisk (*) indicates an original article in THE JOURNAL. Page numbers in the index refer to the bold face numbers in the text.

This is a subject index and one should, therefore, look for the subject word with the following exceptions: Foundations, Lectures, Moving Pictures, and Prizes, under "F," "L," "M," and "P" respectively. "Book Reviews," "Deaths," and "Societies" are indexed under these titles at the end of the letters "B," "D," and "S." Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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Acad.—Academy
Am.—American
A.—Association
Coll.—College
Commn.—Commission
Comm.—Committee
Conf.—Conference
Cong.—Congress
Dist.—District
Div.—Division
Found.—Foundation
Hosp.—Hospital
Indust.—Industrial
Inst.—Institute
Internat.—International
M.—Medical
Med.—Medicine
Nat.—National
Pharm.—Pharmaceutical
Phys.—Physicians
Soc.—Society
Surg.—Surgery
Surgs.—Surgeons
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